FRACTURE PATTERNS

A. J. BUHR
B.A., M.D. Univ. Western Ontario
REGISTRAR RESEARCH ASSISTANT, THE ACCIDENT SERVICE

A. M. COOKE
D.M. Oxon., F.R.C.P.
PHYSICIAN, THE RADCLIFFE INFIRMARY, OXFORD

IN the past thirty years smallpox, diphtheria, the enteric fevers, and rickets have practically been eliminated in this country. In their stead we have new virus diseases, radiation hazards, and the diseases of degeneration. In the elderly, cardiovascular degeneration, strokes, diabetes, osteoarthritis, and fractures present problems as pressing as the great infections did a few decades ago. Medicine can meet these challenges by adapting itself to new situations as they arise, and by preparing to meet the diseases of the future. It is also important that the concern of medical men with the details of diagnosis and treatment should not exclude from their minds the questions—how did the patient come to be so afflicted, and what could have been done for prevention? In so common a condition as fractures such inquiries reveal various facts of interest.

The present study arose from the question put to one of us—are fractures in the aged becoming more common? A pilot survey of the number of fractures of the femur from the head to the subtrochanteric level, admitted to the Radcliffe Infirmary from 1938 to 1955 inclusive, was made (fig. 1). The upper end of the femur was chosen because such fractures almost inevitably make the patient seek medical advice, and nearly always result in admission to hospital. The fractures studied were all traumatic and did not include pathological fractures (e.g., from carcinoma, Paget's disease, or bone cysts). Of the 1434 patients, 70% were female and 30% male, and there was a rise in numbers, the cases in the last year being more than six times as numerous as those in the first year. It was recognised that many factors might have contributed to this rise. The total admissions to the Radcliffe Infirmary doubled between 1938 and 1955; Oxford was a reception area for evacuees in the 1939–45 war; an accident service was established in 1941, which naturally tended to attract fractures to this hospital; and since the war the permanent population of Oxford City has increased by over 12%. Nevertheless, a factor of six times seemed well above any increase, temporary or permanent, in the population.

The fracture figures were then broken down into ten-year age-periods (fig. 2). Below the age of 50, the fractures occurred mostly in males, who presumably suffer more trauma than females; but above that age there was a sharp increase in women, and by the decade 70–79 years, there were four times as many women as men. Below 50, men outnumbered women by 3 to 1, and above that age the ratio was reversed. The drop in numbers after the age of 79 is due to the smaller numbers at risk. A main feature of the age-distribution of the population of England and Wales is a rapid falling-off in numbers after the age of 60, so that there are only about half a million women and a quarter of a million men over the age of 80, as against about 3 million in each of the earlier ten-year age-groups. The figures for 1951 are shown in fig. 3. Fig. 4 shows the data of fig. 2 related to the numbers at risk in each decade—that is, the age-specific rates. Two assumptions have been made: (1) that the age-distribution of the population of Oxford and district is not much different from that of England and Wales as a whole, and (2) that the population figures for 1951 do not differ greatly from those of 1938–55. Both these assumptions admittedly introduce errors, but these are not large enough to make any serious differences to the general shape of the graphs. It must be emphasised that the numbers to the left of the diagram indicate ratios only and not absolute numbers. Our figures suggest that a man of over 80 has a liability to fracture the neck of his femur over thirty times as great as a man of under 40, and a woman of over 80 more than three hundred times that of a woman of under 40. The magnitude of these factors suggests that the bones must be extremely fragile in the aged, and specially in old women, and further suggests that many such fractures are due to atrophied bone rather than to injuries of any severity.

This view is supported by the work of Ghormley, Sutherland, and Pollock (1937) who in a study of patho-

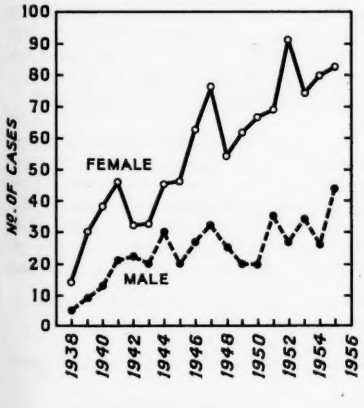


Fig. 1.

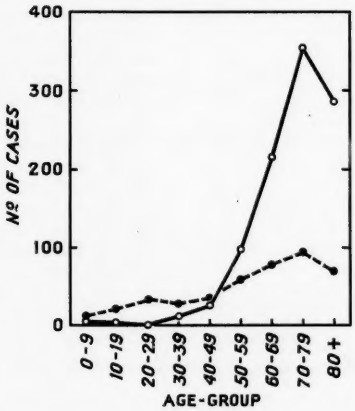


Fig. 2.

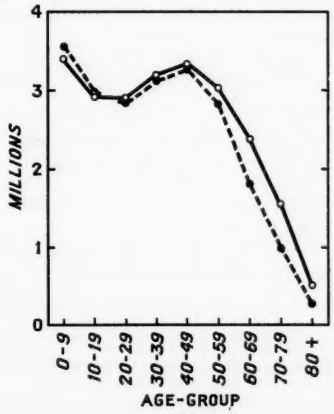


Fig. 3.

Fig. 1—Annual admissions of fractures of the femur, from the head to the subtrochanteric level, to the Radcliffe Infirmary, 1938-55 inclusive.

Fig. 2—The age-distribution of the fractures shown in fig. 1.

Fig. 3—The age-distribution of the population of England and Wales in 1951.

logical fractures found that of those arising from non-malignant conditions, one-third were due to senile osteoporosis, a cause three times as common as the next largest group. More direct evidence was provided by Rutishauser and Dufour (1950), who sectioned the neck of the uninjured femur in six patients who had died after fractured neck of femur, and in every case found osteoporosis. Stewart (1957) in a study of 388 patients with fractured neck of femur found that 27 of them fractured the neck of the other femur on return to activity—no doubt from osteoporosis due to age and aggravated by immobilisation from the first fracture. The preponderance of women with fractured neck of femur conforms with the observed fact that in the 800 published cases of spinal osteoporosis there were six times as many women as men (Cooke 1955).

Material

It was then decided to study other common fractures in a similar manner, and for various reasons the years 1953 to 1957 inclusive were chosen. The total of fractures studied was over 8500, but here we shall give only representative figures. We have purposely kept the classification of the fractures as simple as possible in order to obtain a general view. No doubt, with larger numbers, information of interest might be obtained by more detailed classification—for example, in the shafts of long bones and the spine. The age-specific rates were calculated from the population figures of England and Wales for 1954. We would here like to record our appreciation of the excellent record system of the accident service of the Radcliffe Infirmary, that made this work possible. The fractures studied are shown in table I.

The age and sex distributions fall into four classes. For convenience and brevity we have designated the first three by the letters A, J, and L (because the curves have some resemblance to the shape of these letters). The fourth class we have called Composite.

Type A

There is a predominance of fractures in males, specially during the wage-earning period, and a relatively small number of females at all ages.

Male/female ratio 3·3/1.

Examples are shown in figs. 10, 11, and 12.

Type J

There are few fractures in the younger age-groups in both sexes, but a high incidence in the older groups, with a preponderance in women.

Male/female ratio 1/1·4.

Examples are shown in figs. 4, 5, and 6.

Type L

The majority of fractures occur in youth, with a male preponderance, and a sharp decline in numbers thereafter, that is, the reverse of the J pattern.

Male/female ratio 2/1.

Examples are shown in figs. 7, 8, and 9.

Composite Type

There is either a double peak in both sexes, or an L pattern in men and J pattern in women.

Male/female ratio 1/1.

Examples are shown in figs. 13, 14, and 15.

Where the number of patients is small in the older age-groups, graphs of the numbers of fractures give a fairly true picture; but where the oldest patients are at all numerous it is necessary to show the age-specific rates in order to indicate the true incidence in the different age-groups.

We suggest that the explanations of the various types of age and sex distributions are:

Type A

Most of the fractures falling into this group arise from injuries at work, and they occur predominantly in the hands and feet.

This is essentially the *wage-earner's* fracture pattern.

Type L

In youth trauma is common in both sexes, but slightly more so in the male. In age the numbers fall because severe trauma becomes much less common, and this group comprises bones that presumably do not become appreciably brittle with age.

This is essentially the *pre-wage-earning* fracture pattern.

Type J

Fractures of this type in the young require considerable violence, which occurs more often in men than women. In later life the bones become thin and brittle in both sexes, but more so in women; hence the increase in both sexes and the crossing of the male and female lines of the graph.

This is essentially the *post-wage-earning* fracture pattern.

Composite Type

There is as yet no obvious explanation for the patterns where there are two peaks, one in youth and one in age for both sexes. Fractures of the lower end of the forearm show a combination of the L pattern for males and J pattern for females, for which we suggest the following explanation. The L component in our series is accounted for largely by fracture-separations of the lower radial epiphysis and also

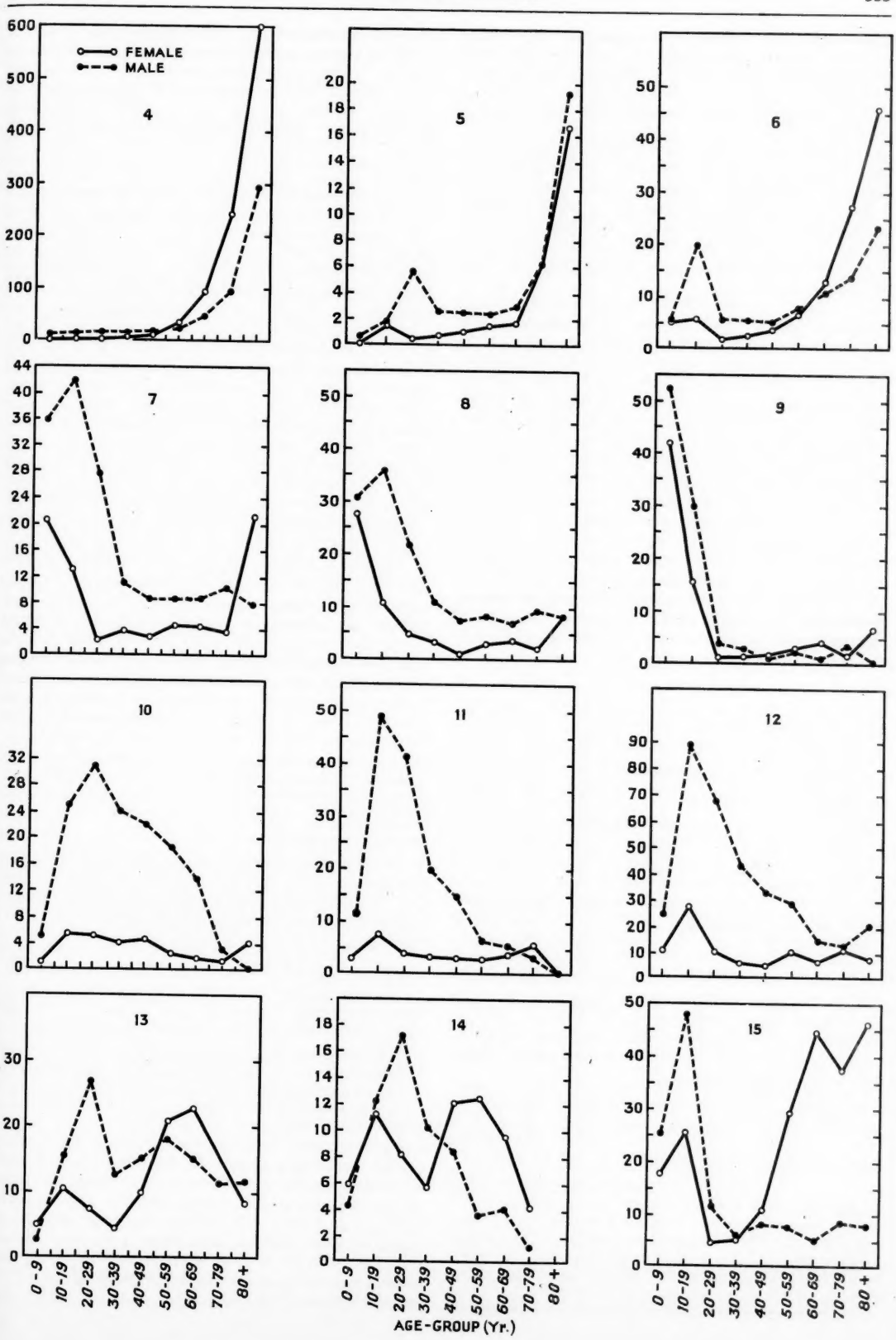
TABLE I—THE FRACTURES STUDIED

—	Male	Female	Total
Upper Extremity:			
Upper end of humerus	179	165	344
Shaft of humerus	46	32	78
Lower end of humerus	303	216	519
Upper end of radius	176	200	376
Lower end of radius and ulna	340	457	797
Carpal bones	330	79	409
Metacarpals	434	84	518
Phalanges	882	226	1108
Lower Extremity			
Upper end of femur	117	321	438
Shaft of femur	128	65	193
Head of tibia	51	37	88
Shaft of tibia	441	172	613
Lower end of tibia only (medial malleolus)	105	41	146
Lower end of fibula only (lateral malleolus)	308	258	566
Tibia and fibula (both malleoli)	87	128	215
Tarsal bones	134	74	208
Metatarsals	289	163	452
Phalanges	401	76	477
Other Bones:			
Clavicle	373	172	545
Ribs	135	40	175
Pelvis	61	35	96
Spine	111	67	178
Totals	5431	3108	8539

LEGENDS TO FIGURES (*facing*)

Figs. 4-15—Age-specific rates per million of population of England and Wales in 1954, showing three examples of each of the fracture patterns described in the text.

4. Femur, head to subtrochanteric level, 1938–55 inclusive.
5. Pelvis. This and all subsequent figures are for 1953–57 inclusive.
6. Upper end of humerus.
7. Shaft of tibia.
8. Clavicle.
9. Lower end of humerus (supracondylar).
10. Phalanges of foot.
11. Metacarpals.
12. Phalanges of hand.
13. Fibular malleolus.
14. Upper end of radius.
15. Lower end of forearm.


FEMALE
MALE
4
5
6
7
8
9
10
11
12
13
14
15
0-9
10-19
20-29
30-39
40-49
50-59
60-69
70-79
80+
AGE-GROUP (Yr.)

includes greenstick fractures of the lower end of the radius and ulna, which overlap slightly with fractures of the lower third of the shaft. The J component represents the true Colles fracture.

The distribution of the fractures according to type is shown in table II.

The characters of these fracture patterns are of course not determined only by the quality of the bones, the degree of violence, and the nature of the injury. There is also the question of the number of traumatic incidents, quite apart from their severity. Sheldon (1948) has pointed out that falls are commoner in old women than in old men, and at ages over 80 there are twice as many falls in the women.

A study of the distribution of the various types of fractures suggests that in age the more vulnerable sites are the predominantly cancellous areas, specially in the ends of the long bones. It seems as though osteoporosis affects the strength of cancellous bone more adversely than that of compact bone. This is not surprising, because when bone atrophies it is removed, lamina by lamina, from all surfaces, internal and external. Removal of a single lamina from compact bone produces a much smaller percentage thinning than removal of a single lamina from the trabeculæ of cancellous bone.

Fractures in the Aged

The social and economic importance of fractures in old age should need no emphasis. In England and Wales $7^1/_2$ million persons are over the age of 60—i.e., 16% of the population. In most hospitals the cost of maintaining an inpatient in a general ward is comparable to the cost of staying in a first-class hotel. It is therefore pertinent to consider the reasons why old people sustain fractures so easily, if only to state the problem before trying to solve it.

TABLE II—DISTRIBUTION OF FRACTURES ACCORDING TO TYPE

—	Male	Female	Total
TYPE A (*wage-earning pattern*):			
Carpal bones	330	79	409
Metacarpals	434	84	518
Phalanges of hand	882	226	1108
Lower end of tibia only (medial malleolus)	105	41	146
Tarsal bones	134	74	208
Metatarsals	289	163	452
Phalanges of foot	401	76	477
Spine	111	67	178
Ribs	135	40	175
Totals	2821	850	3671

—	Male	Female	Total
TYPE J (*post-wage-earning pattern*):			
Upper end of humerus	179	165	344
Shaft of humerus	46	32	78
Upper end of femur	117	321	438
Tibia and fibula (both malleoli)	87	128	215
Pelvis	61	35	96
Totals	490	681	1171

—	Male	Female	Total
TYPE L (*pre-wage-earning pattern*):			
Lower end of humerus	303	216	519
Shaft of tibia	441	172	613
Clavicle	373	172	545
Totals	1117	560	1677

—	Male	Female	Total
Composite Type:			
Upper end of radius	176	200	376
Lower end of radius and ulna	340	457	797
Shaft of femur	128	65	193
Head of tibia	51	37	88
Lower end of fibula only (lateral malleolus)	308	258	566
Totals	1003	1017	2020

The reasons may be considered in three, admittedly arbitrary, groups: (1) the age to which the patients survive, (2) the " external " causes, and (3) the " internal " causes.

Age

The prospect of life of a child born in this country today is about 25 years more than that of a baby born a hundred years ago. This increase is largely due to a reduction in infant mortality and the virtual abolition of the great infections, and until 1950 the prospect of life of both men and women aged 50 was little different from that of a hundred years ago. In the past decade, good medical care, antibiotics, a high standard of living, and an interest by the State and the medical profession in geriatrics have combined to prolong some lives and so give us an increasingly aged population. However admirable this may be on humanitarian and personal grounds, it has led to mankind living longer than Nature intended or has legislated for. Osler's remark about the comparative uselessness of men over 40 and the complete uselessness of men over 60 has a sound biological foundation, and the price that we have to pay for survival to old age is endurance of the involutional changes of age, of which bone atrophy is a prominent one.

How right was Cicero (44 B.C.) when he referred to " Old age . . . which all men wish to attain and yet reproach when attained ".

" External " Causes

These are external to the patient, or in the patient but external to the bones. Although old persons do not sustain much major trauma, they do sustain much minor trauma, chiefly falls. These would have no serious effects in the young, but in the brittle aged they cause fractures. Sheldon (1948) has listed six common causes of such falls:

General muscular weakness.
Arthritis of the lower-limb joints.
Minor pyramidal tract lesions.
Paralysis agitans.
Syncopal attacks.
" Premonitory falls ".

These causes are all self-explanatory except the last, by which is meant the falls that occur because the patient is unwell, usually at the beginning of some febrile illness, such as a respiratory or urinary infection.

Other factors that play a part in falls are:

Unexplained falls, so-called " drop seizures ".
Failing eyesight.
Bifocal spectacles.
Defective hearing.
Slow reaction-time.
Vertigo.
Impaired vibration sense in the lower limbs.
Obstacles in the house, such as furniture, rugs, and pets.
Slippery floors and slippery baths.
Impaired coordination in the dark.
Leaning backwards.

Attention was drawn to the last factor by Sheldon (1948). In falling forwards, the fall can often be checked or broken by the use of the arms, whereas in falling backwards, unless the balance can be regained, the subject falls heavily. Old people find great difficulty in regaining their balance, even when it is only slightly disturbed. There is thus a particular danger in their leaning backwards, as for example in reaching up to fix a curtain or hang a picture.

There seems little doubt that severe trauma mostly occurs in youth, and that minor trauma occurs throughout life but has its serious effects only in the aged.

"Internal" Causes

The chief of these is bone atrophy. Measurement of total skeletal weight (Ingalls 1931) shows that after the age of 55 there is a steady decline in the amount of bone in the body. Histological examination of compact and cancellous bone at various ages seems at first to show that in old age there is solely a diminution in the amount of bone and not any change in its quality. In the elderly, the trabeculæ of cancellous bone are of normal laminar structure but thinner, and in compact bone there is a diminution of volume and increased porosity from enlargement of the haversian canals. Although histology shows that in old age the laminæ appear normal in structure, and chemical analysis shows that the calcium and phosphorus content is normal, analysis also shows that the water content of the matrix of old bone is less—30% in young bone and 20% in old bone (Robinson 1952). This process of dehydration with age is common to all connective tissue. The process of ageing in bone therefore involves changes in both quantity and quality. As a corollary, there must be two kinds of osteoporosis: (1) simple atrophy with no change in the quality of the bone, as occurs in immobilisation of the young, and (2) atrophy plus senile matrix, as seen in old age.

Most methods of testing the mechanical strength of bone for comparison between youth and age use static forces, whereas in real life bones sustain fractures from dynamic forces (Evans 1957). Moreover, such testing methods tend to apply forces in the manner of gravity and take no account, on the one hand, of the complicated stresses caused by muscular action, and, on the other hand, of the stabilising and protective action of muscles and ligaments on bone.

The ageing in bone is usually ascribed variously to age itself, immobilisation, nutrition, and endocrine causes, or combinations of these. With regard to the first of these factors, we are woefully ignorant of the basic causes of ageing, and it would be profitless here to speculate on whether they are mainly determined by genetic, chemical, or endocrine causes. The factor of immobilisation is better understood, and it is generally held that a person confined to bed for upwards of three weeks goes into negative nitrogen, calcium, and phosphorus balance from atrophy of muscles and bones, and that these processes are accelerated by injury and sepsis.

The factor of nutrition is more obscure and controversial. It seems obvious that if the body is not supplied with the basic ingredients for making bone there would be a danger of bone atrophy, specially in view of the fact that some part of the skeleton is always being slowly dissolved away. Series of cases have been published to show that the incidence of osteoporosis is higher in starvation (Eliot and Jackson 1933), in low-calcium intake (Owen, Irving, and Lyall 1940, Vinther-Paulsen 1953), and in multiparous as compared with nulliparous women (Kesson, Morris, and McCutcheon 1943). Nevertheless in such patients there are probably often other factors, such as immobilisation and senile hormonal changes, which may also be playing a part. Information on the relationship of nutrition to osteoporosis is badly needed.

Of the six endocrine glands known to affect bone metabolism, the ovary and testis seem most relevant to the present discussion. Laurence and Riddle (1916) found that the plasma-phosphorus of laying hens was twice as high as in cocks and non-laying hens, and Riddle and Reinhart (1926) found that in pigeons and doves the serum-calcium was more than twice as high as normal during ovulation. Kyes and Potter (1934) described the phenomenon of hyperossification in pigeons, where large amounts of calcium are stored in the hollow long bones in anticipation of the needs of the shell gland for secreting a shell on the egg. These effects were shown to be due solely to œstrogens. The anabolic effects of androgens include in some species stimulation of bone growth. There are considerable species differences in the action of the sex hormones on bone; but it happens that in man, as in the pigeon and dove, both œstrogens and androgens have a bone-building effect. These facts were first applied to the treatment of human beings by Albright, Bloomberg, and Smith in 1940, and hormonal treatment has been extensively used for patients with postmenopausal and senile osteoporosis of the spine, on the whole with beneficial effects. It is probable that the osteoporotic bones of elderly women are related firstly to the fact that the menopause in women is more abrupt than the gradual decline in sexual activity that characterises ageing men; secondly to the fact that of the steroids excreted in the urine, total œstrogen in women shows the sharpest and most consistent decline about the menopause (Pincus 1956); and thirdly to the fact that the susceptibility of the skeleton to the action of œstrogens declines with age (Silberberg and Silberberg 1956).

It is thus probably an oversimplification ever to say that any particular fracture was caused by a specific factor; in most cases the causes are multiple and complex.

Prevention

It is difficult to suggest remedies when the nature of the disease is not even understood. We present our own findings in the hope that further similar studies may be carried out. The only suggestions that might reasonably be made are (1) that fractures in the young are mostly due to "external" causes and might be reduced by attention to the dangers of the roads and in industry, and (2) that fractures in the aged might be reduced by improved physical surroundings, attention to nutrition, mobilisation, and in selected cases endocrine therapy. As regards the physical surroundings, 28% of accidents in the home can be traced to defective design or maintenance of stairs, handrails, lighting, and the like (Interdepartmental Committee 1953).

The kind of inquiry that we have attempted to make, apart from its general biological interest, could be applied to other diseases, and if extended in space and time might give information of value in planning for hospital requirements and bed distribution in the future.

Summary

1. A study of over 8500 fractures of common types has been made, with special reference to age and sex distribution.

2. Study of the age-specific rates shows that the fractures fall into four characteristic patterns:

The *pre-wage-earning* pattern shows a large incidence in both sexes in youth, with a rapid fall to small numbers in middle and later life, resembling the letter L.

The *wage-earning* pattern shows a high incidence in male patients during the working period with a low incidence in youth and old age, and a small number of female patients throughout, resembling the letter A.

The *post-wage-earning* pattern shows a slight preponderance in males in youth, and a striking rise in both sexes in old age, specially in female patients, resembling the letter J.

The fourth group shows a *bimodal pattern* for which there is no obvious explanation at present.

3. The causation of fractures in the elderly is discussed.

We are grateful to Mr. J. C. Scott, director of the accident service at the Radcliffe Infirmary, for his interest, and for providing facilities for this investigation.

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OBSTRUCTIVE JAUNDICE AND HÆMOLYTIC DISEASE OF THE NEWBORN

THOMAS E. OPPÉ
M.B. Lond., M.R.C.P., D.C.H.
LECTURER IN CHILD HEALTH

TIMOS VALAES
Dip. Med. Athens, D.C.H.
REGISTRAR IN PÆDIATRICS

From the University Department of Child Health, Southmead General Hospital, and the South West Regional Transfusion Centre, Bristol

JAUNDICE in hæmolytic disease of the newborn is a consequence of excessive erythrocyte destruction occurring at a time when the ability to conjugate bilirubin is not fully developed. The bile-pigment present to excess in the blood and tissues is, therefore, predominantly unconjugated bilirubin * (Billing and Lathe 1958). But it has been known for some time (Still 1927, Hawksley and Lightwood 1934) that the hæmolytic icterus of erythroblastosis may be accompanied or succeeded by signs of obstructive jaundice. This association has become widely known as the " inspissated bile syndrome " (Hsia et al. 1952), but no systematic studies have been recorded regarding its pathogenesis or its specific position in relation to the total picture of hæmolytic disease.

Since we became interested in this problem we have been able to follow from birth a series of cases of hæmolytic disease with associated obstructive jaundice. Our experience has convinced us, not only that these cases form a specific group, but also that they require special management in the neonatal period. Their study also reveals interesting information concerning the natural history of hæmolytic disease and the metabolism of bilirubin in early life.

* Throughout this paper the terms unconjugated bilirubin and bilirubin refer to the indirect-reacting bile-pigment, and the term conjugated bilirubin refers to the direct-reacting bilirubin which is believed to have been transformed into bilirubin mono- and di-glucuronides within the liver cells.

Material and Methods

During the period Jan. 1, 1957, to Aug. 31, 1958, we studied 117 cases of hæmolytic disease of the newborn due to rhesus incompatibility. These cases were all treated at Southmead Hospital, and the great majority were born there. 10 babies were stillborn. 44 (42%) of the 107 liveborn infants did not need exchange transfusion, and of the 63 infants requiring exchange transfusion 12 showed obstructive jaundice. 4 infants died during the neonatal period, and 3 of these were in the " obstructed " group. This experience can be summarised as follows:

Rhesus hæmolytic disease, total	117
Stillbirths	10 (8·5%)
Neonatal deaths	4 (3·5%)
Total perinatal mortality	14 (12%)
Cases not requiring exchange transfusion	44; deaths 0
Cases requiring exchange transfusion:	
(*a*) Not obstructed	51; deaths 1 (2%)
(*b*) Obstructed	12; deaths 3 (25%)

Infants were designated as showing obstructive jaundice if at the peak of the jaundice at least a third of the total serum-bilirubin was in the conjugated form.

The serum-bilirubin determinations were performed in the department of pathology by a modification of the method of Malloy and Evelyn. The direct (conjugated) pigment was estimated separately, distilled water being substituted for methanol. Calibration curves were constructed from standard solutions of bilirubin (Roche Products Ltd.). Maternal Rh antibody titres were determined at the South West Regional Transfusion centre. Titres recorded (see table) are those obtained by the indirect anti-globulin technique and refer to the serum dilution which existed before the red-cell suspension was added. As a simplification of technique and to minimise errors from " carry-over ", the mother's serum was diluted to 1 in 5 with 0·9% saline solution and then doubly diluted to 1 in 10, 1 in 20, 1 in 40, and 1 in 80.

Results

Consideration of the 12 cases with large amounts of conjugated bilirubin in the blood show that they have many common features. In fig. 1 their cord-blood hæmoglobin and total serum-bilirubin values are com-

SUMMARY OF MAIN FEATURES OF CASES WITH OBSTRUCTIVE JAUNDICE

Case no.	Maternal [titre, 1 in	Gest. age (weeks)	Birth-weight (g.)	Sex	Cord-blood			No. of ex. transf.	Max. serum-bilirubin (mg. per 100 ml.)		Cortico-steroids	Duration of jaundice (days)	Follow-up (mos.)
					Hb (%)	Serum-bilirubin (mg. per 100 ml.)			Total	Direct			
						Total	Direct						
1	40	39	2608	F	47	7·5	4·1	1	24·0	16·0	Cortisone	14	18
2	80	?40	2977	F	44	16·8	9·9	1	38·8	26·5	Cortisone	17	12
3	40	39	3570	F	38	10·8	7·5	1	18·0	14·6		Died at 43 hr.	
4	40	38	3630	F	76	6·8	2·8	1	19·4	14·4	Prednisolone	14	6
5	80	38	2325	F	63	..	..	2	22·0	8·0	Prednisolone	5	9
6	80	37	2636	M	46	5·2	3·3	1	31·0	19·5	Prednisolone	14	9
7	40	38	2580	F	46	11·1	9·0	1			Died at 8 hr.		
8	40	37	2551	F	48	10·8	2·2	2	25·5	18·0	None	17	7
9	80	38	2976	M	71	9·4	5·3	2	51·0	28·0	None	22	6
10	10	39	2550	F	42	12·2	6·5	1	22·5	14·4		Died at 20 hr.	
11	20	40	2770	F	Born at home			1	28·3	11·0	None	10	..
12	40	37–38	2500	M	32	9·7	6·6	1	29·5	20·0	Cortisone	35	..

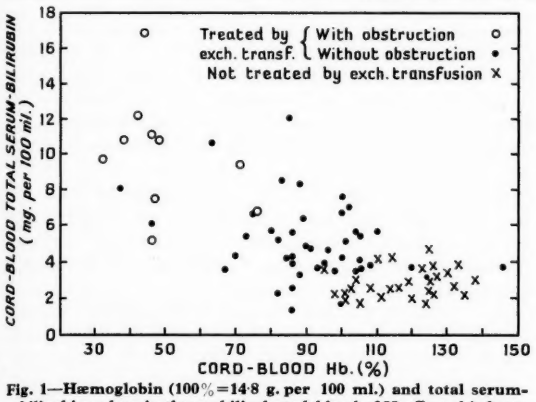
Treated by exch. transf. { With obstruction / Without obstruction
Not treated by exch. transfusion
CORD-BLOOD TOTAL SERUM-BILIRUBIN (mg. per 100 ml.)
CORD-BLOOD Hb. (%)

Fig. 1—Hæmoglobin (100%=14·8 g. per 100 ml.) and total serum-bilirubin values in the umbilical cord-blood of 82 affected infants, showing the severe degree of anæmia and hyperbilirubinæmia associated with impending obstructive jaundice.

pared with those in infants without obstruction. Infants destined to show obstructive jaundice show at birth gross anæmia and hyperbilirubinæmia. The homogeneity of the obstructed group is confirmed in the accompanying table, which shows their main clinical and hæmatological features. The observation by Lathe (1955) that infants with obstructive jaundice have large livers was confirmed, and we found that the degree of hepatosplenomegaly closely reflected the severity of the subsequent obstructive element. Only in our mildest case (case 9) was considerable hepatosplenomegaly not found at birth, and, except for the 2 immature infants referred to later, none of the non-obstructed babies showed equivalent enlargement of the liver and spleen.

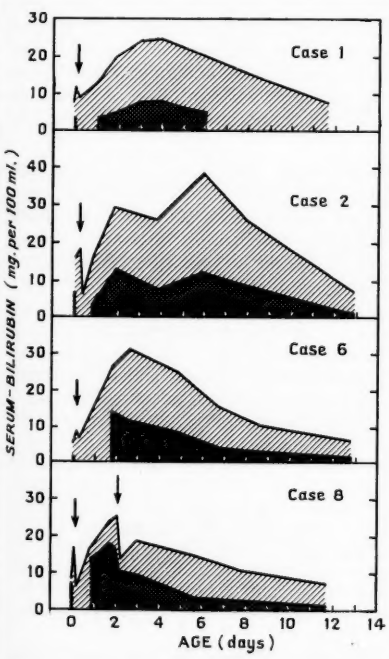

Fig. 2—Changes in serum-bilirubin levels with age in cases 1, 2, 6, and 8. The black shading indicates unconjugated bilirubin and the hatched area total serum-bilirubin; conjugated bilirubin is represented by the difference between the two. Arrows indicate exchange transfusion.

The illness ran a typical course as illustrated in fig. 2 (cases 1, 2, 6, 8) and fig. 3 (case 9). At birth more than 2 mg. conjugated bilirubin per 100 ml. was found in the cord-blood—a level of conjugated bilirubin never found in cases not developing obstructive jaundice. Despite the early adequate exchange transfusions which the obstructed babies received (60–80 ml. per lb. body-weight within four hours of birth), hyperbilirubinæmia increased, reaching a maximum at about the 5th day. The icterus could be distinguished from that of uncomplicated hæmolytic disease by its greenish hue and the presence of bile in the urine. The stools were sometimes paler than normal but were not completely acholic. Hæmorrhages into the skin or lungs were observed in 2 cases, and hypoprothrombinæmia was demonstrated. This responded to parenteral potassium menaphthosulphate (' Vikastab '). The jaundice was long-continued, decreasing over two to three weeks, and the decline in jaundice was accompanied by parallel reduction in liver size. Despite the severity of the hæmolytic disease, no case received more than two exchange transfusions. As we became aware that the syndrome of obstructive jaundice was related to the severity of hæmolytic disease and the intensity of erythropoiesis, further evidence was sought on the capacity of these infants to produce erythrocytes.

Case 9 was unusual in that the cord-blood hæmoglobin was considerably higher than that of the others in the series. There were 28% reticulocytes in the cord-blood and at 3 days there

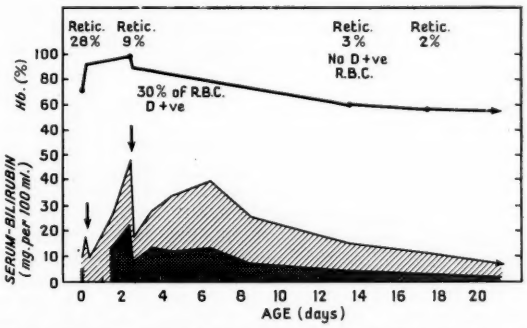

Fig. 3—Case 9: changes in serum-bilirubin level, Hb, reticulocytes, and proportion of D-positive red blood-cells (R.B.C.). Shading as in fig. 2.

were 30% D-positive red cells in the peripheral blood after two large exchange transfusions.

Case 12 was extremely ill at birth with gross anæmia, cardiorespiratory distress, and raised venous pressure. A small exchange transfusion (65 ml. per lb. body-weight with 40 ml. deficit) improved his condition, but the obstructive jaundice ran a protracted course. Serial hæmatological examinations showed intense erythropoietic activity:

Day of life	*Hb* (%)	*Reticulocytes* (%)	*D-positive erythrocytes* (%)
Cord	32	16	100 (assumed)
3	119	4	5
8	112	2·5	30
15	102	<1·0	10
26	92	5·0	30
32	72	6·5	60

The postmortem findings in the fatal cases showed the changes associated with severe erythroblastosis, including bile thrombi. Extramedullary erythropoiesis was a notable feature in the sections of liver examined.

Discussion

Therapeutic intervention has greatly modified the course of erythroblastosis and icterus gravis neonatorum. It is, therefore, not easy to relate to present experience earlier references to obstructive jaundice in hæmolytic disease.

The reviews of Lightwood and Bodian (1946) and Harris et al. (1954) show that, in untreated or partly treated cases of hæmolytic disease, obstructive jaundice was not uncommon and was often severe and long-continued. Two main hypotheses on the pathogenesis have been advanced. In the

severe cases which died before or soon after birth the green-staining of the liver was thought to be due to liver-cell damage, while in cases of long-continued obstructive jaundice simulating atresia of the bile-ducts or neonatal hepatitis the obstruction was regarded as a consequence of inspissation of bile in the bileducts. Hsia et al. (1952) supported the " inspissated bile syndrome " hypothesis, but commented that, as the use of exchange transfusion had become more widespread, fewer cases of long-continued jaundice were seen. Cornblath et al. (1955) showed that increased amounts of conjugated bilirubin were present at birth in obstructed cases; and Stempfel et al. (1956) confirmed this in twelve cases and showed that in adequately treated cases the obstructive phase was transient.

We contend that obstructive jaundice is not due primarily to damage to hepatic cells or to bile thrombi, although both these may develop as sequels. We believe that the obstructive jaundice is related in predictable fashion to the severity of the initial hæmolytic process, and that the degree and duration of the obstructive phase is modified by early and adequate treatment. Obstructive jaundice is consistently found in those severely affected infants who have suffered from the greatest amount of hæmolysis in utero. They have large livers, owing probably to extramedullary erythropoiesis. It is probably the distortion of the bile canaliculi by the extensive areas of erythropoietic tissue that causes the obstruction to bile flow. When the anæmia is corrected and hæmolysis decreased by exchange transfusion, the necessity for continued erythropoiesis is lessened and there is a decrease of liver size concomitant with the liberation of bile flow. Any profound disturbance of liver function in these babies is unlikely, because of their demonstrated ability to conjugate bilirubin and the normality of their course following treatment. If the condition were due primarily to mechanical plugging of bileducts (" inspissated bile ") we would expect the obstructive element to be negligible at birth and to be much more exacerbated by the postnatal hyperbilirubinæmic crisis.

The failure of biliary excretion leads to hyperbilirubinæmia and clinical obstructive jaundice. The contribution to the icterus of hæmolytic disease by the " obstructive " element is conjugated bilirubin, and there is no evidence that the water-soluble mono- and di-glucuronides of bilirubin are neurotoxic. It is, therefore, reasonable to discount conjugated bilirubin as a factor in the production of kernicterus. In our cases high levels of conjugated bilirubin have been permitted, and no infant has shown clinical evidence of kernicterus either in the neonatal period or at follow-up. On the other hand, if the total serum-bilirubin is assumed to consist of unconjugated bilirubin only, there is a real risk of unnecessary and potentially dangerous repeated exchange transfusions being undertaken. The presence of clinical obstructive jaundice (bilestained urine, greenish-yellow icterus) does not relieve the pædiatrician of his responsibility to perform exchange transfusion if the level of unconjugated bilirubin rises to dangerous heights or the infant shows the slightest clinical signs of kernicterus.

We suggest that the conjugated bilirubin should be estimated separately in the cord-blood of all infants in whom severe hæmolytic disease is anticipated. If this value cannot be obtained, anæmia, hyperbilirubinæmia (total), and hepatosplenomegaly at birth are highly suggestive of impending obstructive jaundice. These babies are likely to show circulatory disturbances and require urgent exchange transfusion to reduce plasma-volume and correct anæmia. At this time, partially packed red cells should be infused with the aim of achieving a post-transfusion hæmoglobin value of 100%, while creating the required negative balance of blood-volume. The object of this initial exchange transfusion is the reduction of venous pressure and correction of anæmia, which can be achieved by an exchange turnover of not more than 80 ml. per lb. body-weight.

Subsequently the infants should be carefully observed for bilestained urine and pale stools, and, in any case, exchange transfusion should not be repeated without ascertaining the precise contributions made by both conjugated and unconjugated bilirubin. If obstructive jaundice is apparent clinically or biochemically a parenteral vitamin-K preparation should be given as prophylaxis against hypoprothrombinæmia. Some of our cases were treated with steroid hormones as we feared that long-continued obstructive jaundice or cirrhosis of the liver might occur. No convincing benefit resulted, and we can no longer find any rationale for their use in these circumstances.

But we do not regard the general question of steroid-hormone therapy in severe hæmolytic disease as settled; and possibly our dosage was inadequate, or follow-up may reveal differences between the treated and untreated cases. We cannot be certain that these infants have escaped liver damage, but no cirrhosis has yet appeared, and liver-function tests performed on some of them were normal.

There are indications that the syndrome of obstructive jaundice in hæmolytic disease has re-emerged as a consequence of recent trends in the management of rh-immunised pregnancies. Timely premature delivery in selected cases has resulted in the prevention of intrauterine deaths, and increased skill in exchange transfusion has led to the survival of gravely ill babies. It is these infants, who formerly died, who appear now to display most often the signs of obstructive jaundice; and further improvements in the survival-rate of erythroblastotic infants will probably increase the number of obstructed cases seen.

In our experience very immature infants, although having close similarities at birth with our obstructed cases, do not display an obstructive phase. This may be because little or no conjugation of bilirubin is possible in the fœtus until about 36 weeks of gestation (Brown and Zuelzer 1958). For example:

Baby A.—Mother aged 29. Previous hydropic stillbirth. Born by cæsarean section at 36 weeks, weighing 1920 g. Cord-blood: Hb 37%; total serum-bilirubin 8·1 mg. per 100 ml. Considerable hepatosplenomegaly, pallor, and cardiorespiratory distress. Treated by two exchange transfusions ($1\frac{1}{2}$ hours and 30 hours after birth). No evidence of obstruction, and free of jaundice by the 5th day.

Baby B (younger sister of case 1).—Labour induced at 36 weeks because of high maternal antibody titre. Female, weighed 2098 g. at birth. Cord-blood: Hb 46%; bilirubin conjugated 1·4, unconjugated 4·7, total 6·1 mg. per 100 ml. At birth she was pale, and had considerable hepatosplenomegaly. Respiratory distress developed. After successful exchange transfusion her maximum total serum-bilirubin was 9·0 mg. per 100 ml. (conjugated 2 mg.). Jaundice disappeared on 3rd day.

The proved ability of the infants in our series to conjugate bilirubin successfully (a capacity said to be deficient in many normal full-term infants) may have been derived from the intense hæmolysis in intrauterine life speeding up through biological necessity the development of the glucuronide-conjugating system which normally lies

dormant throughout fœtal life. Unfortunately evidence as to the dynamics of bilirubin metabolism in fœtal life is hard to obtain.

Summary

12 cases of severe hæmolytic disease of the newborn with associated obstructive jaundice detectable at birth are described.

Early, adequate exchange transfusion is the most important factor in management. Biliary obstruction does not contribute toward kernicterus but may lead to hypoprothrombinæmia, which should be prevented. Failure to recognise this clinical entity may result in unnecessary repetition of exchange transfusion.

These cases represent a definite clinical entity within the spectrum of disease caused by rhesus incompatibility.

We are grateful to the obstetricians and pædiatricians at Southmead Hospital for their cooperation and interest. Our thanks are due to Dr. G. H. Tovey, in whose department the serological and hæmatological determinations were performed, and who gave valued advice during the work and in the preparation of the manuscript. Dr. F. J. W. Lewis supported us throughout by his interest and the provision of consistently reliable biochemical estimations.

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ASPIRIN AND GASTRIC HÆMORRHAGE

A. MUIR
M.R.C.P.
CONSULTANT PHYSICIAN, SOUTH LANARKSHIRE GROUP

ISABEL A. COSSAR
M.B. Edin., D.C.H.
JUNIOR HOSPITAL MEDICAL OFFICER,
LAW HOSPITAL, CARLUKE, LANARKSHIRE

IT has been known for twenty years that salicylates and allied compounds may produce gastric hæmorrhage. Douthwaite (1938), Douthwaite and Lintott (1938), and Hurst and Lintott (1939) all reported this fact. In four years Hurst (1943) saw 51 patients whose gastric bleeding had no evident cause, and in about half of them he attributed it to aspirin.

Dodd et al. (1937), Honigberger (1943), Caravati and Cosgrove (1946), Gross and Greenberg (1948), and Ivy et al. (1950) thought that the form of salicylate taken made little difference to its gastric effect, because the drug acted through the blood-stream, after its absorption. This was generally accepted until our own investigations were published in 1955. We came to the conclusion that of every eight episodes of gastroduodenal hæmorrhage, one was caused by local aspirin irritation, usually producing an acute erosive gastritis.

Paul (1943), Wolf and Wolff (1943), Waterson (1955), and Allibone and Flint (1958a) did not agree. But the conclusions of Allibone and Flint have been firmly criticised by Acheson (1958) and they themselves have recently admitted that some of their contentions were wrong (Allibone and Flint 1958b).

Brown and Mitchell (1956) found that 72% of a series of patients with gastroduodenal hæmorrhage had just taken aspirin. Stubbe (1958) showed a 70% incidence of occult bleeding in 180 patients receiving aspirin. Lange (1957) reported that in patients with gastroduodenal hæmorrhage, the proportion who had taken aspirin before the bleeding was 37% in those with peptic ulcer and 56% in those with negative radiological findings. He regarded aspirin as particularly dangerous in elderly patients with a long history of addiction to it. Schneider (1957), in six out of ten persons studied, found gross bloodstaining in every specimen of an aspirin test-meal.

Alvarez and Summerskill (1958) incriminated salicylates in over 40% of 103 consecutive patients admitted to hospital with gastroduodenal hæmorrhage attributed to peptic ulcer (chronic or acute). They found too that half the patients who took salicylates lost blood in their stools—these patients including cases of peptic ulcer and X-ray-negative dyspepsia and controls. They found no evidence that soluble calcium aspirin is any less irritant than insoluble aspirin.

It is fair to say that most people who have studied this problem agree that aspirin causes gastroduodenal bleeding more often than is generally supposed. The relatively high incidence of aspirin dyspepsia has never been in much doubt.

Pathology

Do patients with duodenal ulcer commonly have an erosive gastritis? The literature on this seemingly simple question is chaotic.

In 256 gastrectomy specimens Magnus (1946) found gastritis only occasionally and it was always mild. The observations of Walters and Sebening (1932) were similar, but Puhl (1927) found gastritis much more frequently. An ulcerative antral gastritis is regarded as commonplace in patients with duodenal ulcer by many European workers (Konjetzny 1930, Christiansen 1940, Tumen and Lieberthal 1943). Schindler (1950) states that in cases of duodenal ulcer the gastric mucosa usually appears normal; but he admits that if the ulcer leads to obstruction " be it spastic or organic, severe gastritis develops rather regularly. It is often the hypertrophic type but other forms of gastritis are seen as well. This mixture of all types of gastritis . . . occurs chiefly in the ulcer bearing stomach, and, if it is distinctly visible one may suspect that the patient has an ulcer."

As a preliminary to our previous studies (Muir and Cossar 1955) we examined 20 stomachs removed for duodenal ulcer, and in none did we see acute erosive gastritis worthy of the name. We therefore agreed with Magnus that it was, at most, a rarity. But since then we have examined many more gastrectomy specimens, and have found acute erosive gastritis in quite a number of cases of duodenal ulcer in which no aspirin had been taken. We have therefore modified our views considerably. We no longer accept aspirin as a cause of gastritis unless this is of a relatively specific type: it must principally affect the lesser curve; it must be erosive or frankly ulcerative in type; and, above all, one or more of the erosions must take the shape of, and contain, a firm adherent particle of aspirin (such erosions often being under rugæ, where they may be invisible to the gastroscopist). These criteria are almost certainly too strict, but it is better that they should be this than wrong. On these criteria, of about 100 gastrectomy specimens which we have so far seen only 18 have shown gastritis which we could firmly attribute to aspirin.

This low incidence is not easily reconciled with the bleeding which unquestionably takes place after aspirin test-meals. Looking at gastrectomy specimens, we have often been surprised at the normality, or near normality, of the gastric mucosa though the patient had taken aspirin and had had blood in every specimen after an aspirin test-meal. May capillary damage perhaps be caused by salicylates absorbed into the blood-stream, as was formerly supposed?

Present Investigation

All patients with gastroduodenal bleeding admitted to our unit between February, 1956, and December, 1957, were questioned closely about aspirin—their previous experience of it, how it affected them, what variety they took, and how they took it. We investigated 106 patients (39 women and 67 men). The presumptive cause of the bleeding is shown in table I. The patients occupying the beds to the right of these patients were used as controls and similarly questioned.

TABLE I—CAUSES OF HÆMORRHAGE

Cause	Males	Females
Duodenal ulcer confirmed radiologically	24	9
Symptoms of duodenal ulcer but X-ray negative	7	4
Gastric or stomal ulcer confirmed radiologically	11	3
Suspected gastric ulcer but X-ray negative	4	6
Acute lesion	17	9
Miscellaneous:		
Hæmophilia	1	..
Congenital fibrinopenia	1	..
Congestive cardiac failure	1	1
? epistaxis	1	..
Hiatus hernia	..	4
Cancer of stomach	..	1
Lymphosarcoma	..	1
Portal hypertension	..	1
Total	67	39

Having come to the tentative conclusion that, if aspirin causes gastroduodenal bleeding, it will probably do so within forty-eight hours, we limited our questions to the use of aspirin in the forty-eight hours before the hæmorrhage (definite melæna or hæmatemesis).

Of the 106 controls, 17 admitted to taking aspirin within forty-eight hours of admission—a much higher proportion than the 5% found in our previous series.

Of the 106 patients with gastroduodenal hæmorrhage, 57 admitted to taking aspirin within forty-eight hours of their hæmorrhage (table II). From so small a series it is easy to draw false conclusions; but it is noteworthy that of 26 patients (" acute lesion " group) who did not give any previous history of dyspepsia and showed no X-ray abnormality, no fewer than 19 had taken aspirin.

The 57 people who had taken aspirin before their bleeding were asked some further questions:

1. *Had they previously noted that aspirin gave them indigestion or intensified existing indigestion?*

Of the 36 patients with presumed peptic ulceration 17 were aware that aspirin made their dyspepsia worse, sometimes actually exacerbating ulcer symptoms if taken in a symptom-free period; 12 had taken aspirin without ill effect; and 7 could not or would not give a definite answer.

Of the 19 patients in the " acute lesion " group, 8 knew from previous experience that aspirin gave them heartburn; 5 had taken it occasionally with impunity; and 6 had never taken any to their knowledge.

TABLE II—CASES IN WHICH ASPIRIN HAD BEEN TAKEN BEFORE THE HÆMORRHAGE

Cause	Males			Females		
	Within 48 hr.	Within 24 hr.	Within 6 hr.	Within 48 hr.	Within 24 hr.	Within 6 hr.
Proved D.U.	5	4	3	1	1	2
Presumed D.U.	2	3	1	1	..	..
Proved G.U.	2	1	4	..	..	1
Presumed G.U.	1	1	..	..	1	2
Acute lesion	4	2	5	3	2	3
Miscellaneous	..	1	..	..	..	..

D.U. = duodenal ulcer. G.U. = gastric ulcer.

2. *How was the aspirin taken?*

Uncrushed with fluid on empty stomach	23
Uncrushed with fluid after a meal	7
In powder form with fluid on empty stomach	14
„ „ „ „ after a meal	3
Combination of one or more of these methods	10

3. *What variety of aspirin was taken?*

B.P. aspirin tablets	36
Proprietary powders containing aspirin	7
Compound aspirin tablets	7
Soluble calcium aspirin	1
Indefinite or more than one type	6

4. *Had the patient suffered from dyspepsia in the interval between taking aspirin and bleeding?*

Ulcer group (36):	
No dyspepsia	4
Usual dyspepsia	17
Dyspepsia particularly severe	4
Indefinite	11
Acute-lesion group (19):	
No dyspepsia	7
Dyspepsia	10
Indefinite	2

5. *Severity of hæmorrhage*

Aspirin-takers	(57)	Transfusion needed	4
Non-aspirin-takers	(49)	„	6

6. *Did the aspirin hæmatemesis group contain more elderly people as Lange suggests?*

Aspirin-takers (57):					
Over 70	10	30–40	5		
60–70	10	20–30	3		
50–60	13	Under 20	4		
40–50	12				
Non-aspirin-takers (49):					
Over 70	9	30–40	5		
60–70	10	20–30	8		
50–60	10	Under 20	1		
40–50	6				

Discussion

About half of a series of patients admitted to hospital with gastroduodenal bleeding were found to have taken aspirin within 48 hours of their first hæmorrhage as compared with 15% of a control series with miscellaneous illnesses. These figures strongly support the contention that aspirin is a potent factor in this type of bleeding. Aspirin had been taken by 23 of the 44 patients presumed to have a duodenal ulcer, by 13 of the 24 presumed to have a gastric ulcer, and by no fewer than 19 of the 26 with no previous history of dyspepsia. These figures agree with our previous ones (Muir and Cossar 1955) if allowance is made for the fact that our earlier investigation covered only the twenty-four hours before the hæmorrhage.

Again it was possible to divide the aspirin-hæmatemesis group into three categories:

1. In 14 patients the history was so definite that no other conclusion could reasonably be reached. 9 were in the acute-lesion group, 4 had a duodenal ulcer, and 1 had a gastric ulcer.

2. In 12 patients (6 duodenal ulcer, 3 gastric ulcer, and 3 acute lesion) the history, though suggestive, left room for doubt.

3. The remaining 31 patients (14 duodenal ulcer, 9 gastric ulcer, 7 no previous dyspepsia, 1 portal hypertension) had taken aspirin within forty-eight hours of their initial hæmorrhage, but their histories gave no clue to whether it was in any way responsible for the bleeding. Many of them had taken aspirin regularly with impunity; some had stories of previous gastric bleeding when no aspirin had been taken and none gave the characteristic story of aspirin/heartburn-and-epigastric-distress/bleeding.

Even if we accept only the first category of patients (14) as true examples of aspirin bleeding, we again come to the conclusion that one patient in every eight admitted with

gastroduodenal hæmorrhage was directly suffering from aspirin intolerance.

The source of hæmorrhage in these patients must be speculative, but we still think that most of the acute-lesion group bled from an acute erosive gastritis.

Further points of interest are:

1. Of the people who bled after taking aspirin, fully half knew that aspirin gave them indigestion. This applies to both the acute-lesion group and the presumed-peptic-ulcer group.

2. Aspirin was much more dangerous when taken on an empty stomach. This is in itself evidence that aspirin is harmful to the stomach. Crushing of the tablets apparently made little difference to its irritant properties.

3. Only 1 patient had taken soluble calcium aspirin ('Disprin') and he was in the third or doubtful class. This seems to us significant, because we know that soluble calcium aspirin is prescribed widely in this area.

4. Before their bleeding, relatively few of the ulcer patients noted any increase in their dyspepsia after taking aspirin whereas half the acute-lesion patients did so. The former finding is at variance with our previous observation that a third of our peptic-ulcer patients disliked aspirin because it increased their indigestion.

5. We cannot support Lange's contention that hæmorrhage from aspirin is more likely in older patients.

This second series convinces us more than ever that aspirin is a dangerous drug, particularly for those in whom it causes indigestion and in those with peptic ulcer. If indeed one gastroduodenal hæmorrhage in eight is caused by aspirin, surely the time has come for a much fuller investigation into its effect on the stomach.

Summary

Of 106 patients admitted with gastroduodenal hæmorrhage, 57 admitted having taken aspirin within forty-eight hours of their initial bleeding. Of 106 patients without gastroduodenal hæmorrhage, 17% had taken aspirin in the forty-eight hours before admission.

The group of patients who most commonly gave a history of taking aspirin before the hæmorrhage were those with acute gastric lesions (no history of dyspepsia).

Of the people whose hæmorrhage followed ingestion of aspirin, half knew that aspirin gave them indigestion.

Aspirin is more dangerous in this respect if taken on an empty stomach.

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ALDOSTERONE EXCRETION AND TISSUE ELECTROLYTES IN NORMAL PREGNANCY AND PRE-ECLAMPSIA

D. KUMAR
M.B. Lucknow

L. A. W. FELTHAM
M.A. Toronto

A. G. GORNALL
Ph.D. Toronto

From the Department of Obstetrics and Gynæcology and the Department of Pathological Chemistry, University of Toronto, Canada

THE increase of aldosterone in the urine during late pregnancy (Venning and Dyrenfurth 1956) is a finding of great interest. If it reflects a high level in the plasma, then the immunity of the normal pregnant woman to her hyperaldosteronæmia calls for an explanation. Dieckmann and Pottinger (1956) have reported that the total muscle-sodium is increased in normal pregnancy, but reverts to the non-pregnant range in pre-eclampsia. Tatum (1956) found no significant difference in the total muscle-sodium of normal and toxæmic patients.

The possibility of defining a relationship between aldosterone excretion and tissue-electrolyte metabolism provided a new approach to the problem, and led to this report.

Clinical Factors

Since aldosterone excretion increases considerably when the sodium intake decreases (Luetscher and Axelrad 1954), it was necessary to keep the patients in hospital under metabolic-ward conditions. Seventeen reliable, intelligent, normal pregnant women in their last trimester were selected at different times from the prenatal clinic of the Toronto General Hospital. As a basal intake each patient had for 12 days a low-salt (1 g. sodium chloride) diet prepared especially for the metabolic ward. Judging from sodium-excretion data, the salt content of this diet was generally satisfactory but occasionally it may have contained up to twice this amount of salt. For 6 of the 12 days (sometimes the first 6, sometimes the last 6) a normal-salt (8 g.) intake was achieved by supplying an additional 7 g. of sodium chloride in three portions, either as tablets or as a 20% solution; one portion was taken by mouth with each meal.

Biopsy specimens of the rectus abdominis muscle were obtained, after the nerves supplying the area had been blocked with 2% procaine solution, on the morning of the 6th day of the controlled dietary period.

About 3 g. of tissue was transferred to a covered weighing bottle, and taken immediately to the laboratory. There the tissue was placed in a humidified cabinet and blotted free of superficial blood; all visible fat and connective tissue was carefully removed. The muscle was then cut into small pieces with scissors, and duplicate representative samples were weighed on a torsion balance for each of the various analyses.

Seven patients with signs of pre-aclampsia and three normal non-pregnant women were investigated in a similar manner; with one exception they were on the normal-salt diet during the test.

Analytical Methods

Muscle.—Part of the muscle was used for sodium, potassium, and water determinations.

The tissue was placed in tared platinum crucibles, dried at 103°C for 48 hours, then cooled and weighed. The loss in weight gave a measure of the water-content of the tissue. The dry tissue was then ashed overnight at 500°C. The ash was diluted appropriately with

water, and sodium and potassium were determined by flame photometry.

Chlorides were determined on another weighed portion of muscle by the Wilson and Ball (1928) modification of Van Slyke's method.

Other pieces of muscle were extracted for fat with a mixture of 3 parts ethyl alcohol and 1 part ethyl ether.

The solution was evaporated, the dry residue extracted with a mixture of 3 parts petroleum ether (*B.P.* 30–60°C) and 1 part chloroform, and after evaporating this extract the residue was weighed.

All our electrolyte values have been corrected for the fat-content of the tissue. The calculation of intracellular data was based on the method of Hastings and Eichelberger (1937), assuming all chloride to be extracellular; the results are believed to be accurate to about ±2 mEq.

Serum.—Blood specimens were obtained at the time of the biopsy. The serum was separated as soon as possible and analysed for sodium, potassium, chloride, and water by methods similar to those described above.

Urine.—All urine specimens were collected under refrigeration and without preservatives. Creatinine determinations were made to check the accuracy of the 24-hour collections. In each normal-salt and low-salt period 24-hour specimens were analysed for 17-ketosteroids (Vestergaard 1951), "free" corticoids (Gornall and Macdonald 1953), total ketogenic corticoids (Appleby et al. 1955), and pregnanediol (Robson and Gornall 1955).

The urine passed on the 4th and 5th days of each 6-day dietary period was pooled and analysed for aldosterone by the procedure of Gornall et al. (1956). If there was to be any delay the specimen was stored in a frozen state. The analysis involved a 2-day continuous extraction at pH 2, followed by chromatographic isolation and spectrophotometric estimation of the aldosterone.

Results

STEROID-EXCRETION DATA

Normal pregnant women.—The 24-hour urinary excretion of 17-ketosteroids, "free" corticoids, and ketogenic corticoids was measured in twelve patients and pregnanediol was measured in ten patients when on normal-salt and on low-salt diets. The results are summarised in table I which also gives the ranges in non-pregnant

TABLE I—24-HOUR URINARY EXCRETION OF HORMONES IN RELATION TO SALT INTAKE IN PREGNANT AND NORMAL WOMEN

—	17-keto-steroids (mg. per day)	"Free" corticoids (mg. per day)	Ketogenic corticoids (mg. per day)	Pregnane-diol (mg. per day)
Normal-salt intake:				
Range	8·0–17·0	1·8–4·9	5·4–18·7	20–58
Mean	11·6	3·3	11·8	42
Low-salt intake:				
Range	7·1–16·2	2·1–4·7	7·1–22·5	16–59
Mean	11·2	3·3	14·2	34
Range in non-pregnant women	6–16	1·5–2·5	5–15	<10

normal women for the methods used. The "free" corticoids on the average were almost twice the normal, probably reflecting a decreased rate of metabolism. The dietary restriction of salt did not affect significantly the excretion of these hormones.

The quantity of aldosterone excreted is shown in table II. Analyses were made in six cases on both the normal-salt and low-salt diets, and in eleven additional cases for one dietary period only. Also included in the table is the average 24-hour output of sodium during the period of urine collection for the aldosterone determination. We assumed that the patients were in balance at this time. As shown, the sodium output on each diet is in fairly good agreement with the reported intake.

TABLE II—ALDOSTERONE EXCRETION IN NORMAL PREGNANCY

Case no.	Normal-salt (8 g.) intake (approx. 140 mEq. sodium)		Low-salt (1 g.) intake (approx. 20 mEq. sodium)	
	Urine sodium (mEq. per day)	Urine aldosterone (μg. per day)	Urine sodium (mEq. per day)	Urine aldosterone (μg. per day)
1	149	40	48	73
2	155	50	28	87
3	120	21	22	111
4	120	125	28	190
5	158	21	33	77
6	122	36	23	66
Average	..	49	..	101
7	..	..	32	82
8	149	50	..	..
9	136	72	..	..
10	150	75	..	..
11	100	35	..	..
12	108	36	..	..
13	120	113	..	..
14	135	70	..	..
15	124	13	..	..
16	..	..	50	50
17	..	..	29	48

Aldosterone averages have been calculated only where determinations were completed in the same patient under the two different dietary regimes. Sodium restriction may evoke a sharp rise in aldosterone excretion even when the value on a normal-salt intake is already very high (case 4).

To see whether there was much diurnal variation in aldosterone excretion by pregnant women, urine from two of these patients was collected in 3 portions (6 A.M.–2 P.M., 2 P.M.–10 P.M., and 10 P.M.–6 A.M.) on 3 consecutive days. Analysis of the pooled collections gave the following results:

Case 13.—51·8, 30·5, and 30·5 μg. per 8 hr.
Case 14.—21·7, 28·5, and 19·9 μg. per 8 hr.

This aldosterone excretion does not appear to diminish to any significant extent during the night.

Normal non-pregnant women.—In the childbearing age, aldosterone excretion by normal non-pregnant women on a daily salt intake of about 8 g. ranged from 4 to 11 μg. per day using our method. The mean for ten women was 8 μg. These values agree with other reports when a comparable procedure has been employed.

Patients with pre-eclampsia.—It is difficult to study patients with mild pre-eclampsia under ideal conditions of controlled dietary intake because pre-eclampsia is usually a reversible, transitional state. In our experience about seven out of ten patients with mild pre-eclampsia, diagnosed according to the American Committee on Maternal Welfare (Eastman 1956), recover rapidly when taken into hospital and given a diet containing 8 g. of salt per day. After allowing for a degree of equilibrium to be achieved on the controlled intake, most of our patients had improved and in some the signs and symptoms of pre-eclampsia had cleared completely. Under the conditions we had set ourselves only mild cases could be studied, and only in this group would it be possible to observe any further development of the toxæmic syndrome. In the more severe pre-eclamptics the urgency of treatment precluded metabolic investigation.

Of the patients studied therefore, only five were still mildly pre-eclamptic when the urine was collected for aldosterone determination. Muscle biopsies were taken from three of them. Two others were investigated in the same way even though their condition had cleared by the time the urine and biopsies were obtained. The aldosterone-excretion data are shown in table III.

In the patients still showing signs of pre-eclampsia the trend appears to be towards lower, not higher, aldosterone values. In the two patients who recovered during the stabilisation period the values are nearer the average for normal pregnant women.

ELECTROLYTE DATA

It is not easy to find normal non-pregnant women who can be kept for 5 or 6 days on a controlled diet, and who will volunteer to permit a muscle biopsy. Table III gives the results on one such case, but our other biopsies on normal women were taken before repair of a simple umbilical hernia. These patients were on the controlled diet containing 8 g. of salt daily for 5 days before the biopsy, which was done under local anæsthesia.

Muscle samples were taken during the 3rd trimester from six normal pregnant women having a normal-salt diet, and from five having a low-salt diet. The electrolyte data for these biopsies are also given in table III.

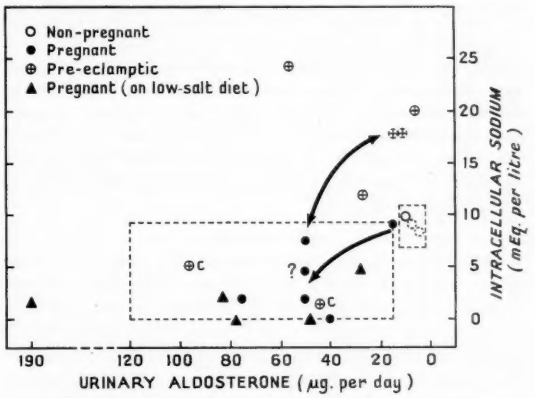
The muscle specimens from the pre-eclamptic patients were taken when their daily salt intake was 8 g. In two cases all signs of pre-eclampsia had cleared at the time of biopsy; the other three patients were still mildly pre-eclamptic though only one (case 25) was retaining

TABLE III—ALDOSTERONE EXCRETION IN NON-PREGNANT, PREGNANT, AND PRE-ECLAMPTIC PATIENTS

Group and case no.	Aldosterone excretion (μg. per day)	Total muscle				Intracellular		
		Water (g. per kg.)	Chloride (mEq. per kg.)	Sodium (mEq. per kg.)	Potassium (mEq. per kg.)	Water (g. per kg.)	Sodium (mEq. per l.)	Potassium (mEq. per l.)
Group A:								
18	10	784	29·1	41·6	84·0	536	10·2	154·8
19	..	770	22·2	31·8	100·5	583	8·4	171·0
20	..	780	29·8	41·9	90·0	510	7·3	174·3
Average	..	778	27·0	38·4	91·5	543	8·6	166·7
Group B:								
1	40	800	30·2	36·3	91·3	548	0·0	164·9
8	50	794	22·5	31·8	89·0	603	7·8	146·2
2	50	785	33·0	41·5	91·1	505	2·0	177·8
16	..	794	25·7	36·2	92·9	571	4·7	161·1
10	75	818	24·7	31·4	94·8	608	2·0	154·8
15	13	796	19·9	29·7	91·7	627	9·3	145·3
Average	46	798	26·0	34·5	91·8	577	4·3	158·4
Group C:								
21	*(27)**	793	22·1	31·3	89·1	603	4·8	146·3
7	82	798	23·7	30·6	87·1	599	2·2	144·1
17	48	814	25·5	27·2	86·9	605	0·0	142·1
4	190	800	22·3	27·8	94·9	611	1·6	154·1
5	77	790	27·1	31·1	87·4	563	0·0	153·4
Average	99 *(85)*	799	24·1	29·6	89·1	596	1·7	148·0
Group D:								
22	96	802	29·4	38·4	93·0	558	5·2	164·3
23	44	806	24·3	31·5	89·7	593	1·5	149·6
Average	70	804	26·8	35·0	91·3	575	3·4	157·0
Group E:								
24	27	802	24·6	37·4	102·2	596	11·9	169·9
25	56	790	23·4	41·9	96·6	601	24·4	159·4
26	6	801	24·0	41·5	90·7	599	20·2	149·7
26 (on low-salt intake)	*(14)*	..	..	..	..	..	..	..
Average	23†	798	24·0	40·3	96·5	599	18·8	159·7

* Analytical difficulties, some losses suspected.
† In addition 2 other pre-eclamptic patients on a normal-salt intake had aldosterone values of 14 μg. and 13 μg. per day respectively, which are included in this average.

Group A = normal non-pregnant women on a normal-salt (8 g.) diet.
" B = normal pregnant women (3rd trimester) on a normal-salt (8 g.) diet.
" C = normal pregnant women (3rd trimester) on a low-salt (1 g.) diet.
" D = pre-eclamptic patients (3rd trimester) on a normal-salt (8 g.) diet (recovered).
" E = pre-eclamptic patients (3rd trimester) on a normal-salt (8 g.) diet (signs still present).



Aldosterone excretion and intracellular-sodium values

The small dotted rectangle and hollow circles are the values from normal non-pregnant women on a normal-salt diet. The large dotted rectangle and solid dots represent values during the normal 3rd trimester of pregnancy in women on a normal-salt diet.

"?" indicates that the aldosterone result is missing and an average figure has been assumed. The circled crosses are the values in pre-eclamptic patients; in the 2 marked "c" the signs had cleared when the tests were made. The crosses indicate 2 patients in whom aldosterone-excretion values only were obtained. The solid triangles indicate the results during the 3rd trimester of pregnancy on a low-salt diet.

significant amounts of sodium. The results of the electrolyte analyses are shown in table III.

The values for total muscle sodium, potassium, and chloride in pregnancy and pre-eclampsia are probably not significantly different from those of normal non-pregnant women. The derived values for intracellular sodium, however, show interesting differences. The average for non-pregnant women appears to be 8–9 mEq. per litre. In the normal pregnant women with a daily salt intake of 8 g. the intracellular sodium ranged from 0 to 9·3 mEq. per litre, which is certainly not above normal, and probably tends to be lower than normal. In our series these figures averaged about half those for the non-pregnant women. Supporting these results in the presence of a high aldosterone output, are the still lower values found in pregnant women on a diet containing 1 g. of salt per day. Here the average was only 1·7 mEq. per litre while the aldosterone excretion doubled.

In the two pre-eclamptic patients who recovered during the stabilisation period the intracellular-sodium values were in the range for normal pregnancy. But the patients who still had signs of pre-eclampsia at the time of biopsy all had intracellular sodium values that were distinctly above normal.

The water-content of the tissues in normal pregnancy and pre-eclampsia was slightly increased.

The trend revealed by these preliminary observations is illustrated in the figure. The small dotted rectangle gives the approximate range of aldosterone excretion and intracellular sodium for normal non-pregnant women on normal-salt diet. The larger dotted rectangle shows the usual range for these two factors in the 3rd trimester of normal pregnancy. The lower arrow indicates the change from an average aldosterone excretion of 8 μg. to 50 μg. per day, and from a mean intracellular-sodium value of about 8·6 mEq. to about 4·3 mEq. per litre of cell water. Included in the chart also are values obtained during the 3rd trimester of normal pregnancy from patients on a low-salt intake.

The trend suggested by our preliminary data in patients still showing signs of pre-eclampsia is indicated by the upper arrow; the intracellular sodium is increased and the aldosterone output tends to fall. The results for the two pre-eclamptic patients who had recovered suggest that the upper arrow should indicate a reversible change. We have not yet been able to determine whether the aldosterone changes precede or follow the alterations in intracellular sodium.

Discussion

Our findings show clearly that aldosterone excretion rises, usually to high levels, during pregnancy. In contrast to the slight increase in urinary cortisol that may occur during pregnancy (de Courcy et al. 1953), which Migeon et al. (1957) and Cohen et al. (1958) explain on the basis of a decreased metabolism, the increase in aldosterone by the 3rd trimester is on the average more than sixfold. When the salt intake is restricted the output is roughly doubled again. These observations suggest that the increased excretion of aldosterone is due in part, and perhaps mainly, to increased production. There is evidence that this arises from the maternal adrenals and not from the placenta or fœtal adrenals (Baulieu et al. 1957, Laidlaw et al. 1958). There is no evidence that diurnal variation is an important factor.

Salt restriction is clearly not responsible for the sixfold or sevenfold rise. A volume-receptor mechanism seems to be excluded by the evidence that the plasma-volume (Tysoe and Lowenstein 1950) and the extracellular fluid-volume (Chesley 1943, Caton et al. 1949) are increased during pregnancy. Œstrogens have been shown to have a striking effect on the plasma level and biological half-life of cortisol (Wallace et al. 1957, Cohen et al. 1958) which may be due to an effect on protein binding of this steroid (Mills 1958). No indication of a similar effect on aldosterone has been obtained. Farrell (1958) has presented evidence for a centre in the mid-brain capable of regulating aldosterone production by liberation of a specific " glomerulotrophic " hormone. The mechanism by which this centre is activated is not yet known.

The vital question seems to be whether the urinary aldosterone released by hydrolysis at pH 1–2 represents a biologically active form of aldosterone in vivo. If so, then the presence of large amounts of œstrogen and progesterone during pregnancy may block the peripheral action of aldosterone. Progesterone has been shown to enhance the renal excretion of sodium (Landau et al. 1955, 1958).

It is conceivable that pregnancy causes in some way a primary increase in production of aldosterone by the adrenals. If, as suggested by Woodbury and Koch (1957), this hormone is capable of removing sodium from muscle cells, one might thus account for the lower intracellular-sodium values found in normal pregnancy. Our data and those of Rinsler and Rigby (1957) and Wolff et al. (1958) indicate a tendency to lower aldosterone-excretion values in patients with pre-eclampsia. Such a decrease might then allow a restoration of intracellular sodium. But it is difficult to account in this way for the very high values of intracellular sodium sometimes found.

Our investigations suggest another possibility. The apparent immunity of pregnant women to aldosterone might be explained if the rise in aldosterone is *secondary* to some endogenous factor which has the effect of lowering intracellular sodium, perhaps in a mid-brain centre. But indications of a correlation between low intracellular-sodium values and high aldosterone excretion were not definite.

If there exists a " cell-sodium-lowering (C.S.L.) factor " in pregnancy, then a compensatory rise in aldosterone would probably be harmless only as long as this factor remained. It follows that the development of pre-eclampsia could be due to chronic intermittent or sudden decreases in the C.S.L. factor during pregnancy. The possibility that the placenta is the source of an antipressor factor (Browne 1958) which may be a C.S.L. factor, or in pre-eclampsia is the source of a factor sensitising the tissues to aldosterone—perhaps by suppressing C.S.L. factor—must be kept in mind. By this hypothesis also the reaccumulation of sodium in the cells would reduce or abolish the stimulus to aldosterone production, and a decreased excretion would be the expected consequence in pre-eclampsia.

Our values for total muscle-sodium in non-pregnant, pregnant, and pre-eclamptic women on the normal-salt diet are in the general range of 30–42 mEq. per kg. of fat-free wet tissue. This agrees with published data so far as the non-pregnant and pre-eclamptic women are concerned. But neither Tatum (1956) nor we have confirmed the finding of Dieckmann and Pottinger (1956) that sodium is increased in the muscles of normal pregnant women. The *intracellular* sodium appears in fact to be lowered in normal pregnancy, and considerably increased in pre-eclampsia.

Summary

Under metabolic ward conditions, at normal (8 g.) and low (1 g.) dietary salt intakes, aldosterone excretion and tissue electrolytes were determined in normal pregnant women. Normal non-pregnant women and patients with signs of pre-eclampsia were studied on a normal-salt intake.

Normal non-pregnant women of childbearing age were found to excrete 4–11 μg. of aldosterone per day on a normal-salt diet. Intracellular sodium values in three such women were 10·2, 8·4, and 7·3 mEq. per litre of cell water. Normal pregnant women in the 3rd trimester were found to excrete 13–125 μg. of aldosterone per day (average 50 μg.) on a similar diet. Intracellular-sodium values in six of these women ranged from 0 to 9·3 mEq., with a mean of 4·3 mEq. per litre. Five similar women on a low-salt diet had intracellular-sodium values averaging 1·7 mEq. per litre, with a mean aldosterone excretion of about 100 μg. per day.

Five patients with pre-eclampsia on a normal-salt diet had aldosterone values ranging from 6 to 56 μg. with a mean of 25 μg. per day. Three of them had intracellular-sodium values of 11·9, 20·2, and 24·4 mEq. per litre. These preliminary findings indicate that in normal pregnancy there is usually a high aldosterone excretion with a tendency to low intracellular sodium, and in pre-eclampsia lower aldosterone values with a tendency to high intracellular sodium.

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References at foot of next column

MECHANICAL PROPERTIES OF THE CHEST DURING INTERMITTENT POSITIVE-PRESSURE RESPIRATION

LIONEL H. OPIE
M.B. Cape Town, M.R.C.P.
RESEARCH ASSISTANT

J. M. K. SPALDING
D.M. Oxon., M.R.C.P.
NEUROLOGIST

RESPIRATION UNIT, DEPARTMENT OF NEUROLOGY

F. D. STOTT
M.A., D.Phil. Oxon.
OF THE M.R.C. EXTERNAL STAFF

From The United Oxford Hospitals

THE study described here was conducted with the cooperation of patients with paralysis or paresis of the respiratory muscles, and we are grateful for their assistance.

Methods

A four-channel direct-writing capacitance manometer * was used to record simultaneously tracheal pressure, œsophageal pressure, tracheal air-flow, and tidal volume. The frequency response is satisfactory up to 15 c.p.s.

All patients had tracheotomies and the "*tracheal pressure*" was measured close to the external end of the tracheotomy tube.

The *œsophageal pressure* was used to indicate intrathoracic pressure (Fry et al. 1952, Howell and Peckett 1957). It was measured either with a water-filled tube using Southern Instruments gauge G231 or an air-filled balloon, using Southern Instruments gauge G247C or G247D. Many patients were fed by stomach-tube, and in these cases it was convenient to attach a polyethylene tube, 1 mm. bore and 100 cm. long, to the stomach-tube so that when the stomach tube was in situ the end of polyethylene tube was approximately in the mid-œsophagus. This œsophageal tube was kept patent by injecting 1 ml. of water down it every two hours, and enabled œsophageal pressures to be recorded with the water-filled system whenever desired, without causing the patients inconvenience. The position of the œsophageal end of the tube was checked before each recording by altering its position until maximal cardiac impulses were obtained on the œsophageal pressure trace, and then withdrawing it for a few centimetres. The reference point was the phlebostatic axis (Winsor and Burch 1946). This is the axis where the plane through the midaxillary line intersects the plane passing at right-angles to this at the level of the fourth intercostal space at the sternal edge.

A second method of recording the œsophageal pressure was used on other patients. This employs an air-filled system, and more readily gives readings of absolute pressure. A polyethylene tube, 1·5 mm. bore, was enclosed over its terminal 18 cm. by a latex balloon 0·6 cm. in diameter, which tolerated the introduction of 2 ml. air when lax and free before any pressure change occurred. Before records were made the balloon was emptied of air and then 1·5 ml. was introduced into it. The part of the polyethylene tube inside the balloon had an aperture in its wall every 2 cm. Initial experience in positioning the balloon was gained with a radio-opaque marker, and later the balloon was passed until it was estimated that its upper end lay 2–5 cm. below the level of the larynx.

Air-flow to and from the trachea was measured by a modified Lilly grid-type flowmeter. Many flowmeters have a large dead space which makes them difficult to use with patients requiring artificial respiration, and one of us (F. D. S.) designed a flowmeter with a dead space of only 25 ml. Calibration (fig. 1) is not quite linear and flow-rates were read off from a calibration diagram.

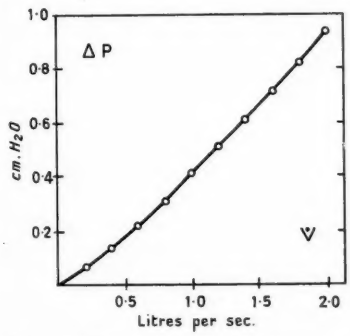

Fig. 1—Calibration curve of flowmeter. Pressure difference (ΔP), flow (V̇).

The differential pressure was recorded with a Southern Instruments differential pressure head, type G247C. This head was fitted with external damping resistances on both sides to achieve approximately critical damping, and at the same time equalise the response-times of the two sides. This is essential when the head is being used in conjunction with intermittent positive-pressure respiration (I.P.P.R.), since otherwise large transient responses are produced from the head by sudden changes of pressure in the system even when there is no flow through the flowmeter tube. Unless this equalisation of response-time is carefully carried out, the transient artefact due to the pressure changes which occur with the respiration pump may be many times greater in amplitude than the true peak flow-rates. The air provided for the patients in our respiration unit is normally humidified. If records of flow lasting any considerable time were contemplated, the humidifier (Marshall and Spalding 1953) was allowed to cool before the records were taken, to prevent the Morrel screen being affected by condensed water.

Tidal volume was recorded by electrical integration of the air-flow signal. The time-constant of the integrator was 30 seconds. It was calibrated against a recording spirometer of known linearity and was found accurate within 4% with flows between 0·5 and 1·5 litres per second and within 13% with flows between 0 and 2·0 litres per second. Except where otherwise stated, all volume and pressure changes were measured relative to the values obtained with the patient's chest in the resting position, and each value represents the average of three readings.

The patients studied had respiratory paralysis or paresis due to poliomyelitis, polyneuritis, myasthenia gravis, or curare used as treatment in severe tetanus. They were receiving I.P.P.R. from one of the Radcliffe respiration pumps (Russell et al. 1956, Sutcliffe and Spalding 1959). Two other patients who were receiving I.P.P.R. for severe bronchitis and emphysema are considered in a separate section. Every patient had a cuffed rubber tracheotomy tube (Spalding and Smith 1956),

* Southern Instruments E 8 and MR 450 Units.

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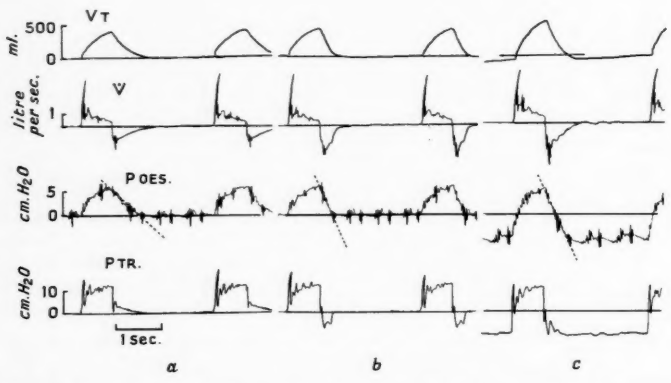

Fig. 2—Records of tidal volume (Vt), tracheal air-flow (V̇), œsophageal pressure (P oes.), and tracheal pressure (P tr.) in a patient with acute poliomyelitis.

In (*a*) there is no negative tracheal pressure during expiration, in (*b*) the negative pressure is very brief, and in (*c*) it persists from the end of one inspiration to the beginning of the next.

and the cuff was inflated sufficiently to provide an air-tight fit in the trachea.

Results

The type of record obtained is shown in fig. 2. The subject of this observation had poliomyelitis of sixteen days' duration, and similar records were obtained from four other patients with acute poliomyelitis, one with acute polyneuritis, and one with tetanus who was curarised. The tracheal pressure is of the "square" form characteristic of the Radcliffe respiration pumps, and this causes the air-flow to rise suddenly to its maximum at the beginning of inspiration.

Intrathoracic Pressure

Any procedure which raises the intrathoracic pressure impedes the venous return to the heart, and, although the healthy subject can compensate for this to a considerable degree, the seriously ill patient may not be able to do so. The mean œsophageal pressure was taken as an index of the obstruction to the venous return.

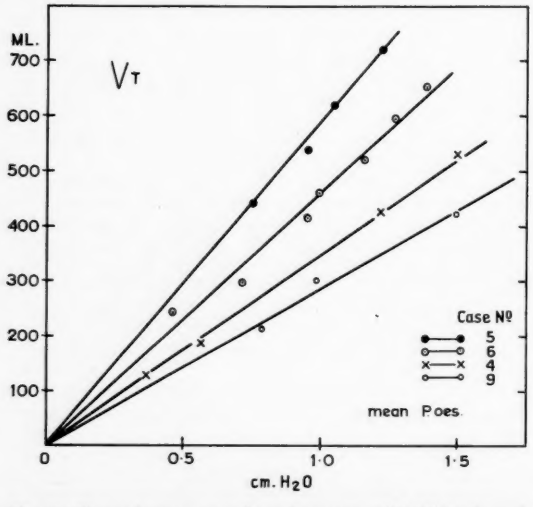

Fig. 3—Change in mean œsophageal pressure with tidal volume in four paralysed patients. Respiratory rate 16 per minute except in case 6, in whom it was 23 per minute.

Our patients were examined supine, and in this position the œsophageal pressure is higher than in the erect position (Howell 1956, Butler 1957). In eight completely paralysed patients the œsophageal pressure with the chest in the resting position—that is, when they were temporarily disconnected from the respirator—was −0·43 cm. water (0·43 cm. water below the atmospheric pressure).

With I.P.P.R. the œsophageal pressure rises during inspiration, and with I.P.P.R. of the type shown in fig. 2 the rise in mean œsophageal pressure varies directly with the tidal volume (fig. 3).

At 16 respirations per minute and with tidal volume of 500 ml. the mean œsophageal pressure in four patients with complete respiratory paralysis rose between 0·86 and 1·78 cm. water (average 1·30 cm. water) compared to the resting pressure. During spontaneous inspiration, on the contrary, the œsophageal pressure falls; and the mean œsophageal pressure in four healthy supine subjects breathing quietly at about 16 respirations per minute, with tidal volume of about 500 ml., fell by 0·80–2·80 cm. water (average 2·40 cm. water) compared to the resting pressure. The patient on

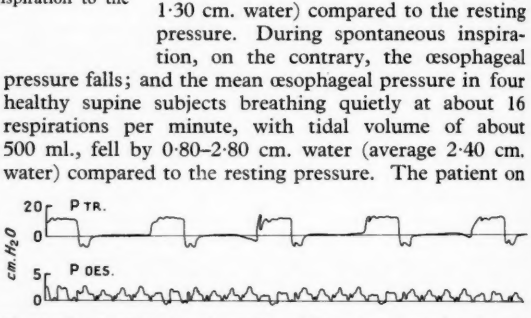

Fig. 4—Tracheal (P tr.) and œsophageal (P oes.) pressures in a paretic patient who is synchronising her respiration with the respiration pump.

I.P.P.R. therefore had obstruction to the venous return from 1·66–4·58 cm. water (average 3·70 cm. water) compared to the normal subject.

When the paralysed patient recovers some respiratory power he rapidly learns to synchronise his efforts with the respirator. Fig. 4 shows tracheal and œsophageal pressures in a girl, aged 15, five days after the onset of respiratory failure due to poliomyelitis. She synchronised so well with the respirator that her œsophageal pressure scarcely varied at any phase of respiration.

Two factors which influence the mean œsophageal pressure are the duration of inspiration and the application of negative pressure during expiration.

With I.P.P.R. of the type considered here, if the *duration of inspiration* is sufficient, inspiratory flow stops (fig. 5); and further extension of the inspiratory period not only fails to increase the tidal volume, but also causes a sustained rise in the intrathoracic pressure, which interferes with venous return. It is therefore important to reduce the inspiratory period as much as possible without unduly impairing the tidal volume. The relationship of tidal volume to duration of inspiration in five patients at various tracheal pressures applied by a Radcliffe respiration pump is shown in fig. 6. For tidal volume of the size normally required in clinical practice an inspiratory period longer than 1·0–1·5 seconds serves no useful purpose. Using a model lung and a variable resistance previously described (Spalding and Young 1955) this conclusion was found to be valid for airway resistances as high as 16 cm. water per litre per second.

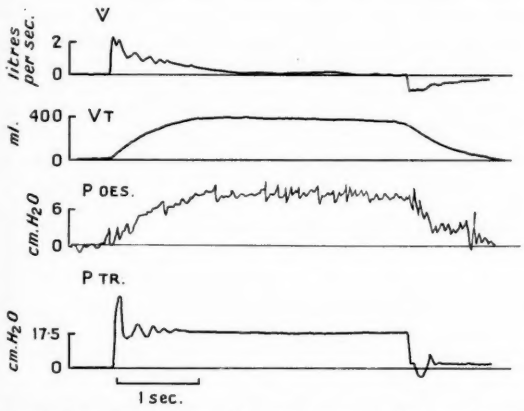

Fig. 5—Tracheal air-flow (V̇), tidal volume (Vt), œsophageal pressure (P oes.), and tracheal pressure (P tr.) of a paralysed patient during prolonged inspiration.

The effect of *negative pressure in expiration* is shown in fig. 2 (b and c). The introduction of short negative-pressure phase immediately after the inspiratory period (fig. 2b) caused some interesting alterations in the air-flow and œsophageal-pressure patterns. In each of six patients the peak expiratory flow was enhanced by about 50%. Their average period of expiratory flow was shortened from 1·63 seconds to 1·06 seconds, and the œsophageal pressure fell more steeply.

When the negative-pressure phase was prolonged to cover the whole of the expiratory period (fig. 2c), the chest was contracted beyond the resting position, and the baseline of the tidal volume record fell below its resting level. The tidal volume was therefore increased, although the peak tracheal pressure was unchanged. The peak flow-rates were also increased. The expiratory decline of œsophageal pressure was as steep as with a brief negative-pressure phase at the onset of expiration. The effect on the œsophageal pressure was striking, for it fell to sub-atmospheric levels during the expiratory period.

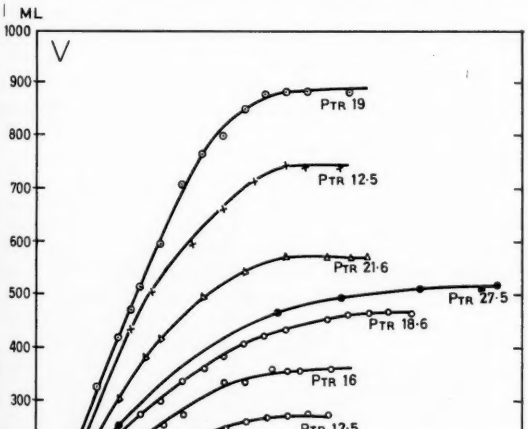

Fig. 6—Relationship of inspired volume (V) to duration of inspiration at various tracheal pressures (P tr.) in five patients. Tracheal pressure is given in cm. water.

In seven patients on I.P.P.R. the œsophageal pressure was measured at a respiratory rate of 16 per minute with tracheal positive pressure adjusted to give tidal volumes between 300 and 500 ml., and no negative pressure. The average mean œsophageal pressure was 1·53 cm. water (range 0·45–2·05 cm. water). With the same positive tracheal pressure and in addition a negative pressure of about 7 cm. water throughout the interinspiratory period, the average mean œsophageal pressure dropped to −0·87 cm. water (range −2·66 to + 0·52 cm. water), and the tidal volume increased by about 150 ml.

Elastic Resistance (Compliance)

The elastic resistance of the whole chest is the force required to hold the chest stationary in a position other than the resting position, and it is expressed as the compliance—that is, the volume of air that can be introduced into the lungs by pressure of 1 cm. water. This pressure-volume relationship is very nearly linear (fig. 7), and it can therefore be determined by a single measurement if necessary. The compliance of the whole chest can be subdivided into two components—the compliance, first, of the lungs and, secondly, of the chest wall. Since the œsophageal pressure is an accurate guide to changes in intrapleural pressure whether the subject is supine or erect (Howell and Peckett 1957), measurements of œsophageal pressure can be used to determine the lung compliance and the chest-wall compliance. Measurements are taken at a time in the respiratory cycle when air-flow has ceased, so that the effect of airway resistance is eliminated. In a paralysed patient receiving I.P.P.R.

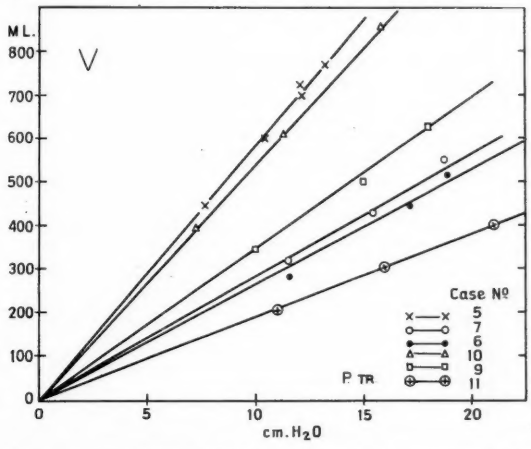

Fig. 7—Inspired volume (V) at various tracheal pressures (P tr.) when airflow has ceased.

$$\text{Whole chest compliance} = \frac{\text{volume (V)}}{\text{tracheal pressure (P tr.)}}$$

By considering the force acting on the lung alone—that is, the trans-lung pressure—we get

$$\text{Lung compliance} = \frac{\text{V}}{\text{P tr.}-\text{œsophageal pressure (P oes.)}}$$

Considering the force acting on the chest wall alone we get

$$\text{Chest wall compliance} = \frac{\text{V}}{\text{P oes.}}$$

TABLE I—COMPLIANCE IN PARALYSED PATIENTS WITH HEALTHY LUNGS

Case no.	Sex	Age (yr.)	Diagnosis	Days on I.P.P.R.	Compliance (ml./cm. H_2O)		
					Whole chest	Lungs	Chest wall
1	F	27	Poliomyelitis	90	32	38	75
2	M	31	Polyneuritis	14	47	62	200
3	M	20	Poliomyelitis	15	27	43	79
4	F	46	Poliomyelitis	About 1 year	25	38	77
5	M	45	Poliomyelitis	1	59	106	135
6	M	11	Poliomyelitis	9	26	41	73
7	M	32	Poliomyelitis	4	28	36	134
				Average	35	52	110

The compliance of seven patients with complete or very severe respiratory paralysis but without major pulmonary abnormality are shown in table I. The average whole-chest compliance is 35 ml. per cm. water, lung compliance 52 ml. per cm. water, and chest-wall compliance 110 ml. per cm. water. Similar measurements in three subjects who had regained some respiratory power are shown in table II. The lung compliance is similar, but the chest wall compliance is much greater, indicating that the patients were actively cooperating with the respiration pump.

In three of these patients the lung compliance was measured both during spontaneous breathing and on I.P.P.R., at an interval of a few minutes (table III). The lung compliance during artificial respiration was generally lower than during spontaneous respiration.

In order to compare the paralysed and paretic patients with normal supine conscious subjects, the lung compliance of four healthy adult male volunteers was determined by a standard method (Comroe et al. 1955). The average was 209 ml. per cm. water (range 103·0–305·0 ml. per cm. water), and these values corresponded closely to those obtained in the same subjects relaxing in a tank respirator.

TABLE II—COMPLIANCE IN PARETIC PATIENTS WITH HEALTHY LUNGS

Case no.	Sex	Age (yr.)	Diagnosis	Days on I.P.P.R.	Vital capacity (ml.)	Compliance (ml./cm. water)		
						Whole chest	Lungs	Chest wall
2	M	31	Polyneuritis	61	1200	52	62	325
8	F	54	Myasthenia gravis	35	800	42	46	455
5	M	45	Poliomyelitis	17	200	43	47	486
					Average	45	52	422

Non-elastic Resistance

When the lungs are inflated, sufficient force is required to overcome not only the elastic resistance of the lungs and chest wall, but also the non-elastic resistance. The greater portion of the non-elastic resistance is due to the narrow air-passages, but a small proportion is represented by the inertia and viscosity of the parts that are moved. The non-elastic resistance is expressed in cm. water pressure per litre air-flow per second, and is conventionally measured at a flow-rate of 0·5 litre per second. The resistance at different flow-rates may be got from a pressure-volume diagram, relating the volume of air introduced to the pressure applied. As with measurements of compliance, the non-elastic resistance can be estimated for the whole chest, and that for the lungs and the chest wall can be determined separately by plotting pressure-volume diagrams using the pressures acting on each structure individually.

The resistance of the chest was measured in three patients receiving I.P.P.R., at tracheal pressures of 15–17·5 cm. water through a right-angled tracheotomy tube of bore 0·8 cm. The average resistance for the whole chest was 4·5 cm. water per litre per second measured during inspiration at 0·5 litre per second (fig. 8). The resistance of the tracheotomy tube was measured during I.P.P.R. with a model lung. It was 2·8 cm. water per litre per second with the tube of bore 0·8 cm., and 1·4 cm. water per litre per second with a tube of bore 0·95 cm. The pulmonary resistance was about 1·2 cm. water per litre per second, and the chest-wall resistance about 0·5 cm. water per litre per second. The chest-wall resistance is very slight and difficult to measure accurately.

TABLE III—COMPLIANCE DURING ARTIFICIAL AND SPONTANEOUS RESPIRATION

Case no.	Sex	Age (yr.)	Diagnosis	Date (1958)	Lung compliance on I.P.P.R. (ml./cm. water)	Lung compliance during spontaneous respiration (ml./cm. water)
2	M	31	Polyneuritis	May 29	92	83
				June 20	108	161
				July 24	52	325
8	F	54	Myasthenia gravis	March 12	46	58
				„ 14	38	89
5	M	45	Poliomyelitis	Aug. 12	71	137
				„ 26	64	124
				Average	68	139

The airway in these patients extended from the site of the tracheostomy to the peripheral branches of the bronchial tree. Comparisons with supine, normal subjects are fallacious unless the upper-airway resistance, from mouth or external nares to trachea, is taken into account. Measurements were therefore made for the upper-airway resistance in three normal male volunteers, free of upper respiratory disease.

A no. 1 Luer needle was introduced through the cricothyroid membrane into the trachea, and the subject breathed spontaneously through a mouthpiece or, keeping his mouth closed, through a mask. Air-flow, tidal volume, and pressure difference between the mask or mouthpiece and the trachea were measured. The average upper-airway resistance to breathing through the nose, measured at 0·5 litre per second, was 1·75 cm. water per litre per

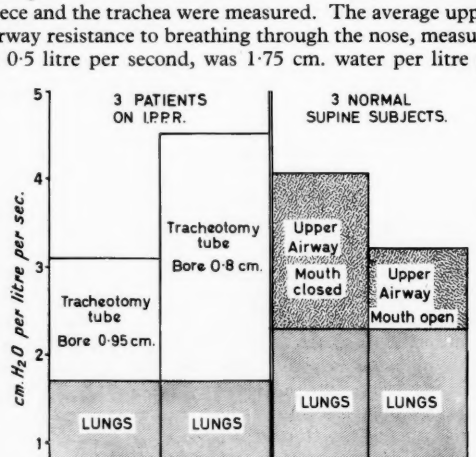

Fig. 8—Non-elastic resistance in patients receiving I.P.P.R. and in normal subjects breathing through nose or mouth.

second, and through the mouth 0·9 cm. water per litre per second. The same subjects, breathing at the same rate through the mouth in the supine position, had a total airway resistance of 3·2 cm. water per litre per second. The pulmonary resistance, which should serve as a basis for comparison for patients with tracheotomies, was therefore 2·3 cm. water per litre per second in these subjects. As the chest wall was actively moving it does not cause resistance.

Pressure Studies in Emphysematous Subjects

Assisted respiration by I.P.P.R. has won recognition as a method of relieving the carbon-dioxide intoxication which develops in advanced pulmonary emphysema (Sieker and Hickman 1956). Two such subjects were studied while receiving I.P.P.R. from Radcliffe respiration pumps.

In both subjects difficulty with the expiratory phase was well demonstrated and, unlike the state in paralysed patients, negative pressure did not hasten expiration (fig. 9). The œsophageal pressure falls very slowly. In one patient flow was measured, and again the use of the negative pressure phase failed either to shorten the duration of expiratory flow or to enhance the peak value reached.

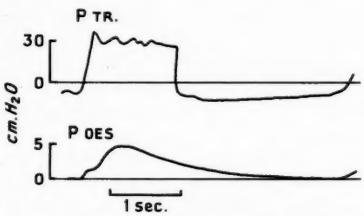

Fig. 9—Tracheal and œsophageal pressure in a patient with severe bronchitis and emphysema treated with I.P.P.R. Negative pressure fails to produce rapid expiration.

Discussion

There are two principle objects in obtaining concurrent records of tracheal pressure, œsophageal pressure, tracheal air-flow, and tidal volume.

The first object is to estimate the effect of artificial respiration on the venous return to the heart. Positive-pressure respiration, and also artificial respiration in a tank respirator (Beck et al. 1952), is a series of minor Valsalva manœuvres. Each inspiration causes a rise in intrathoracic pressure relative to the pressure on the surface of the body, and this tends to impede venous return to the heart. Normal subjects are able to compensate for this, but sick subjects may not have sufficient vascular control to do so (Beecher et al 1943, Maloney et al. 1953, Berneus and Carlsten 1955) and cardiac input and output therefore fall, sometimes disastrously. It is therefore important to consider the ways in which artificial respiration can be carried out effectively with the minimum strain on the circulation.

The second object is to study the mechanical properties of the lungs and to compare then with similar investigations in the normal subject (Mead and Whittenberger 1953, Heaf and Prime 1956). This is possible only because changes in the œsophageal pressure accurately reflect changes in the intrapleural pressure (Dornhorst and Leathart 1952, Fry et al. 1952, Mead et al. 1955). The force acting on the lung (that is, the difference between the tracheal and intrapleural pressures, or "trans-lung pressure") can therefore be obtained, as can the force acting on the chest wall—namely, the difference in pressure inside and outside the chest wall. In the present investigation the œsophageal pressure was measured with the subjects supine, and in this position this pressure is almost 2 cm. water higher than in the erect position (Howell 1956, Butler 1957).

VENOUS RETURN TO THE HEART

One criterion for a good I.P.P. respirator is that it should ventilate the lungs satisfactorily with the minimum strain on the circulation. As fig. 2 shows, the Radcliffe respiration pump gives a "square" type of pressure curve in the trachea, the inspiratory pressure rising to its maximum almost immediately. Inspiratory air-flow rapidly reaches its peak so that the tidal volume is introduced in a short time and the period of raised intrathoracic pressure can be kept short. Inspiration has been arranged to occupy a quarter to a third of the respiratory cycle, 0·9–1·25 seconds at respiratory rate of 16 per minute and, as fig. 5 illustrates, further prolongation of inspiration increases the mean intrathoracic pressure without significantly increasing the ventilation. These findings confirm previous conclusions on the duration of inspiration (Spalding 1955).

The flow pattern during passive expiration is virtually a mirror image of that during inspiration (fig. 2a), and expiratory flow is usually complete in 1·5–1·75 seconds. There is therefore an appreciable pause—0·75–1·0 second—between the end of expiration and the beginning of inspiration. This satisfactory situation is partly due to the small resistance offered to expiration by the mechanically operated expiratory valve.

The introduction of even a short negative pressure at the beginning of expiratory phase has several interesting effects (fig. 2b). Although the same peak œsophageal pressure is reached during the inspiratory period as with positive pressure alone, yet the rate of expiration is increased and, as the time taken for the œsophageal pressure to fall to the resting level is reduced, the mean œsophageal pressure falls by an average of about 20%. The peak expiratory flow is increased by about 50%, often reaching about 2 litres per second, which corresponds to about 10 metres per second or 23 m.p.h. in the trachea. These figures compare with a peak flow-rate of about 0·5 litres per second in normal breathing and 7 litres per second during forced spontaneous breathing (Comroe et al. 1955).

If negative pressure in the trachea is continued until the beginning of the next inspiration (fig. 2c) the flow pattern is not greatly altered, but the mean œsophageal pressure is reduced below atmospheric. It is about −0·87 cm. water compared with about −1·8 cm. water in the normal subject, both measurements being made with the subject in the supine position. Moreover, with prolonged negative pressure the expiratory position of the chest is more collapsed than the resting position, so that for a given peak pressure the introduction of negative pressure between inspirations increases the ventilation but decreases the intrathoracic pressure.

These considerations are likely to be important in the acutely ill and severely paralysed patient. In the patient who has some power of respiration, the ability to synchronise with the respiration pump (fig. 4) lowers the intrathoracic pressure appreciably.

MECHANICAL PROPERTIES OF THE LUNGS

Elastic Resistance (Compliance)

Most investigators have examined subjects in the erect posture, but those who have examined supine subjects have found the chest more compliant than the present series.

The compliance of the *lungs* in our patients with total respiratory paralysis was 52 ml. per cm. water. In our four normal supine subjects it was 209 ml. per cm. water. In four normal supine subjects examined by Howell and Peckett (1957) it was 154 ml. per cm. water, and in those reported by Attinger et al. (1956) 137 ml. per cm. water. Ferris et al. (1952) examined patients with poliomyelitis who were being treated in tank respirators, and the lung compliance was 71·7 ml. per cm. water. Possibly the low compliance in the paralysed patients' lungs is partly due to many small areas of collapse or consolidation in the lungs, too small or transitory to show radiographically, associated with the patient's inability to cough, but this is not the only factor. We examined paretic patients when breathing spontaneously and when receiving I.P.P.R., the two examinations being only a few minutes apart. The average compliance on I.P.P.R. was less than half that during spontaneous breathing. Howell and Peckett (1957) also examined supine patients breathing spontaneously and, a few hours later, when anæsthetised and paralysed. They too found a considerable fall in compliance. We agree with these workers that an alteration in the distribution of inflation of the lungs is the likely cause of the lower compliance in the patients receiving artificial respiration.

The compliance of the *chest wall*, 110 ml. per cm. water, was also less than that found by Howell and Peckett (1957), 174 ml. per cm. water, in their anæsthetised and paralysed subjects. The patients with chronic poliomyelitis examined by Ferris et al. (1952) had a chest-wall compliance of 122 ml. per cm. water.

It is a familiar fact to clinicians caring for patients receiving artificial respiration that, if pulmonary infection develops or if a bronchus becomes blocked, it is more difficult to inflate the patient's lungs. It is possible to express this quantitatively by measuring the whole-chest compliance, which can be done with a capsule-type manometer and a spirometer, both of which are normally available where such patients are treated.

Non-elastic Resistance

The non-elastic resistance of the *lungs* is almost entirely due to the resistance produced by the air-passages. In our three patients with very severe respiratory paralysis the average non-elastic resistance of the lungs, 1·2 cm. water per litre per second, is lower than that of our three normal supine subjects, 2·3 cm. water per litre per second. The normal values for the sitting position are 1·2–3·4 cm. water per litre per second (Comroe et al. 1955, Marshall 1957); but it has previously been observed that in the supine position the value is raised by about 1 cm. water per litre per second (Attinger et al. 1956).

A high resistance in paralysed patients might have been expected, for it is difficult to keep the airways of such patients quite free from occlusion by secretion. Possibly the square wave form of the tracheal pressure provided by the Radcliffe respiration pump may dilate the air-passages and so lower the resistance. If this is so, the resistance will be lower when higher tracheal pressures are employed, and investigations now in progress suggest that this is so.

The "*chest wall*" resistance is only about 0·5 cm. water per litre per second. The figure indicates the viscous resistance and inertia of the chest wall and of those abdominal structures that are moved when the diaphragm is depressed. It cannot be measured on normal subjects whose chest wall and diaphragm are moving actively.

The resistance of the *tracheotomy tube* varies inversely with the fourth power of the bore (Poiseuille's law). This emphasises the importance of using as large a tracheotomy tube as is practical, so that the resistance is comparable with that of the normal upper airway.

PATIENTS WITH BRONCHITIS AND EMPHYSEMA

The above conclusions are applicable to almost all patients with respiratory paralysis, but require considerable modification if the patient has severe bronchitis and emphysema. This is important, for recently I.P.P.R. has been introduced as a treatment of this condition in its acute exacerbations. Inspiration may be very much slower, but this can readily be overcome by increasing the inspiratory pressure. Expiration, however, is notably slowed so that it may not be complete before the next inspiration. This results in a permanently raised intrathoracic pressure which may be undesirable in these patients, who are often already on the verge of circulatory failure. Moreover, in them the application of negative pressure may be useless or even harmful, owing to the trapping effect (Nunn 1958). This is due to the collapse of the walls of diseased bronchi because the pressure is higher in the alveoli around them than it is within their lumen.

Summary

Information has been obtained about the effect of artificial respiration on the circulation and about the mechanical properties of the chest, by the use of a four-channel capacitance manometer. In patients paralysed or paretic from disease simultaneous measurements have been made of tracheal pressure, œsophageal pressure, tracheal air-flow, and tidal volume.

In the paralysed patient receiving intermittent positive-pressure respiration (I.P.P.R.) from a Radcliffe respiration pump the mean œsophageal pressure is 1·66–4·58 cm. water (average 3·70 cm. water) higher than in normal supine subjects. Venous return to the heart is impeded by this amount. Introduction of a negative-pressure phase in the trachea of 7 cm. water throughout the interinspiratory period reduces the mean œsophageal pressure nearly to that of the normal supine subject, and also increases the respiratory minute volume.

The elastic resistance of the chest is greater in the patient receiving I.P.P.R. than in normal supine subjects, or in the same patient breathing spontaneously. This is attributed to alteration in distribution of inflation.

The non-elastic resistance is less in patients receiving I.P.P.R. than in normal subjects. This may be due to dilatation of the bronchial tree by the type of artificial respiration used.

The resistance of the tracheotomy tube is approximately the same as that of the normal upper airway.

We wish to thank Dr. H. G. Epstein and Dr. A. Crampton Smith, of the Nuffield Department of Anæsthetics, for much valuable assistance; Dr. W. Ritchie Russell, director of the Department of Neurology, for encouragement and advice; and Dr. Robert Marshall, of the Nuffield Department of Surgery, for helpful criticism. This work was carried out when one of us (J. M. K. S.) was receiving grants from the Nuffield Committee for the Advancement of Medicine and from the Medical Research Council, and one of us (L. H. O.) was holding a Rhodes scholarship at Lincoln College, Oxford.

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USE OF GEL DIFFUSION PRECIPITATION TEST IN THE DIAGNOSIS OF ADENOVIRUS INFECTIONS

MARGUERITE S. PEREIRA
M.B. Aberd.
OF THE VIRUS REFERENCE LABORATORY, COLINDALE, LONDON, N.W.9

H. G. PEREIRA
Dr. Med. Brazil

A. C. ALLISON
M.A., B.M., D.Phil. Oxon.
OF THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH, MILL HILL, LONDON, N.W.7

SEROLOGICAL studies of adenovirus infections have been carried out by various methods including serum neutralisation, complement fixation (Huebner et al. 1954, Hilleman et al. 1955), sensitised red-cell agglutination (Friedman and Bennett 1957), and conglutinating complement adsorption (Prier and Le Beau 1958). The results of serum neutralisation tests are type-specific, and 23 virus types have so far been identified by them (Rowe et al. 1958). The remaining tests, on the other hand, give group-specific reactions, except when standardised hyperimmune animal sera are used (Pereira 1956, Binn et al. 1958).

Adenovirus antibodies have been found in a high proportion of sera from normal populations, and the application of serological methods to the diagnosis of infection is based on the demonstration of antibody rises in pairs of acute and convalescent sera. The type of virus causing infection cannot be determined with certainty except by virus isolation, since heterotypic antibody responses are often encountered even in serum neutralisation tests.

In the present work, adenovirus antibodies have been detected by the agar-gel diffusion precipitation test described by Ouchterlony (1948). The results were found to be closely related to those obtained by complement fixation.

Materials and Methods

Gel diffusion precipitation tests were performed in petri dishes (6 cm. diameter) each containing 10 ml. of 2% agar in *M*/15 phosphate buffer pH 7·2–7·4 with *M*/100 versene. Wells 7 mm. in diameter were cut with the unit described by Mansi (1957) giving a central and six surrounding wells. The edges of the central and surrounding wells were 4 mm. apart. The bottom of each well was sealed by adding a drop of melted agar.

The antigen was an adenovirus type-5 preparation obtained from HeLa-cell cultures and partially purified by the fluorocarbon compound technique (Gessler et al. 1956) according to the method described by Pereira and Valentine (1958). The central well of each plate was filled with antigen (approximately 0·07 ml.) and each serum to be tested was added to one of the surrounding wells. The plates were left at room temperature for two days before the final reading of the test was recorded. Precipitation lines could best be seen by oblique illumination in a darkroom.

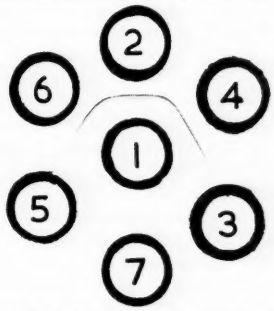
Complement-fixation tests were performed by methods previously described in detail (Pereira 1956) using 0·1 ml. unit volumes and overnight fixation at 4°C.

The sera tested were (*a*) miscellaneous sera sent to the pathological laboratory of Salisbury General Hospital for various diagnostic tests during 1956 and 1957, and (*b*) acute and convalescent sera from cases of adenovirus infections, all confirmed by laboratory tests, and occurring sporadically or in school and military outbreaks.

Adenovirus type-5 antiserum was obtained from a rabbit with a latent infection resulting from a single virus inoculation given intravenously (Pereira and Kelly 1957). Anti-HeLa-cell serum was obtained from a hyperimmunised rabbit given six intravenous doses of a washed HeLa-cell suspension. All sera were inactivated at 56°C for thirty minutes.

Results

Precipitation reactions between adenovirus type-5 antigen and a homologous rabbit antiserum and two sera from patients convalescing from infections by adenovirus types 3 and 5 are shown in the figure. This is contrasted with the negative results given by acute sera from the same patients and by an anti-HeLa-cell rabbit serum. The continuity of the main precipitation line demonstrates the close similarity of an antibody in each of the three positive sera and the group-specificity of the reaction. In addition, the rabbit serum shows a second line.



Gel diffusion precipitation reactions.

1. Adenovirus type-5 antigen.
2. Adenovirus type-5 rabbit antiserum.
3. Acute and (4) convalescent sera from patient infected with adenovirus type 5.
5. Acute and (6) convalescent sera from patient infected with adenovirus type 3.
7. HeLa-cell rabbit antiserum.

Results of the gel diffusion precipitation test were closely related to those of the complement-fixation test, as shown in table I. Positive precipitation tests were obtained with the great majority of sera having complement-fixation titres higher than 1/80 and with very few of the sera having lower titres.

The possible application of the gel diffusion precipitation test to the diagnosis of adenovirus infections was investigated in a series of paired acute and convalescent

TABLE I—CORRELATION BETWEEN COMPLEMENT-FIXATION AND GEL DIFFUSION TESTS IN UNSELECTED HUMAN SERA

C.F.T.*	Gel diffusion test			
	Positive	Negative	Total	% positive
⩽10	1	75	76	1·3
20	1	21	22	4·5
40	1	29	30	3·3
80	10	11	21	47·6
160	10	3	13	76·9
⩾320	14	1	15	93·3

* Reciprocal of serum dilution giving 50% complement fixation.

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sera from patients observed either as sporadic cases or in school and military outbreaks. Diagnosis of adenovirus infection was based on clinico-epidemiological findings and on 4-fold or higher rises in complement-fixing adenovirus antibody in paired sera. The diagnosis was confirmed by virus isolation in 11 cases. The virus types responsible for infections included types 3 (6 cases), 5 (1 case), 7 (3 cases), and 14 (1 case). The results of gel diffusion precipitation tests are shown in table II. Positive results were obtained with all but 2 of the convalescent sera. Precipitation lines

TABLE II—GEL DIFFUSION PRECIPITATION TEST IN PAIRED SERA WITH 4-FOLD OR HIGHER RISES IN ADENOVIRUS COMPLEMENT-FIXING TITRES

	Gel diffusion test				
Acute serum ..	−	−	+	+	Total
Convalescent serum	−	+	+	−	
Number	2	20	4	0	26
%	7·7	76·9	15·4	0	100

in the acute sera were observed in 4 cases, but appearance of these lines occurred later than with the corresponding convalescent sera. Adenovirus type 3 was isolated from both patients whose convalescent sera gave negative results. Full details of these 2 patients are not available, and no explanation for the negative results with the gel diffusion test can be offered at present.

Comments

The gel diffusion technique described above can be simplified for routine diagnostic use. The precipitating antigen can be rendered non-infective by heating at 56°C for thirty minutes. Use of partially purified antigens is not essential, since similar results have been obtained with antigens prepared from virus-infected HeLa cells homogenised by freezing and thawing or by grinding in a Ten Broeck tissue-grinder.

It should be noted that the results of gel diffusion tests were read after one and two days. When the plates were left for longer periods, lines were occasionally seen with previously negative sera. Moreover, even at two days more than one precipitation line was sometimes observed. These have also been found with sera from immunised animals and their significance is under study.

Summary

Adenovirus antibody was detected in human sera by means of the gel diffusion precipitation test. The results of this test were closely related to those obtained by complement fixation. The simplicity of the method suggests its use for the routine serological diagnosis of adenovirus infections.

We are indebted to Dr. B. E. Andrews for the supply of some of the pairs of sera included in this study.

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PATHOGENESIS AND TREATMENT OF THE ANÆMIA ASSOCIATED WITH HIATUS HERNIA

GEORGE J. MICHAELIDES
M.D. Athens
SUPERINTENDENT
H. CHR. PHILIS
RESIDENT
From the 2nd Medical Clinic, University of Athens, Greece

THE cause of the anæmia which occasionally complicates hiatus hernia remains uncertain, but some evidence points to disturbed gastric secretion as an important ætiological factor. Causes which have been suggested include blood-loss, achlorhydria, and blocking of the available iron by the inflammatory exudate; but none of these is always present.

Bleeding is one of the cardinal symptoms of hiatus hernia: of a series of 100 cases Morein (1937) reported hæmatemesis in 21, melæna in 17, and anæmia in 23. He attributed the bleeding to coexistent peptic ulceration, to superficial erosions of the intrathoracic gastric mucosa, or to chronic œsophagitis. Repeated efforts to vomit may also cause bleeding.

Achlorhydria is not very common. Although Murphy and Hay (1943) found anæmia in 70% of their cases, free HCl was increased in most of these. However, when it is diminished, this can be incriminated as a cause of anæmia. The role of HCl in converting trivalent to the more easily absorbed bivalent iron is well established. The polymolecular particles of iron hydroxide in food are converted to single molecules of ionisable trivalent compounds (Gardika 1954); and these are reduced to bivalent iron ions by exogenous reducing substances, such as ascorbic acid or cystein, or by a factor secreted in the stomach. On the other hand, cases of achlorhydria in which iron is still absorbed prove that free HCl is not a sine-qua-non of iron absorption.

Chronic œsophagitis can cause anæmia by repeated bleeding or by trapping the iron of food and using it in the inflammatory reaction.

In a patient treated in our clinic none of these factors could be blamed. He required an operation for the repair of his hiatus hernia; and we took the opportunity to perform a series of tests on him with various iron compounds and reducing substances. Similar tests were carried out on normal controls and on a patient with Banti's syndrome.

Case-report

History

A farmer aged 56 entered the clinic on March 3, 1957. He complained of extreme weakness, palpitations, dizziness, tinnitus, constipation, and vomiting after meals. These symptoms had started five months earlier and were accompanied by progressive anæmia. The patient also complained of food sticking behind the middle of his sternum; and swallowing sometimes produced a splash which he himself could hear. He reported no bleeding of any kind.

He had had malaria at 22 and bacillary dysentery at 24. He had also had two profuse epistaxes five years previously and a hypertensive episode in August, 1956. On this latter occasion his blood-pressure rose to 190 mm. Hg systolic, with headache, dizziness, and vomiting, followed by loss of consciousness. In retrospect the episode was attributed to irritation of the phrenic nerve by spasm of the diaphragm (Bockus 1947).

Physical Findings

Positive findings were his extreme pallor, brittle nails, dullness and diminished air-entry at the left base, a smooth

tongue, and a palpable liver. His pulse was 100 per minute and his blood-pressure 130/90 mm. Hg. His general state of nutrition was good, there was no abdominal tenderness, and the central nervous system showed nothing abnormal.

Fig. 1—Barium meal showing herniation of fundus and part of the body of the stomach into the chest.

Laboratory Findings

Blood examination showed: hæmoglobin 4 g. per 100 ml.; red-cell count 2,230,000 per c.mm.; hæmatocrit 14%; mean corpuscular volume 64 cμ; mean corpuscular hæmoglobin 18 μμg.; mean corpuscular hæmoglobin concentration 28%; white-cell count 5600 per c.mm. (polymorphs 80%, lymphocytes 19%, eosinophils 1%); platelet-count 142,000 per c.mm.; reticulocyte-count 9·6%. The blood-film showed hypochromia, anisocytosis, and poikilocytosis. The bleeding-time was 2 minutes; the coagulation-time was 4–6 minutes; and the clot-retraction and prothrombin-consumption were normal. Serum-iron was 20 μg., serum-siderophilin 425 μg., and serum-copper 116 μg. per 100 ml. The bone-marrow-iron was 0.

TABLE I—IRON ABSORPTION AFTER FERROUS GLUCONATE, FERROUS SULPHATE, AND FERRIC CHLORIDE BY MOUTH

Tests 1–3		1. 176 mg. Fe^{++} gluconate	2. 176 mg. Fe^{++} as sulphate	3. 176 mg. Fe^{+++} as chloride
Serum-iron (μg. per 100 ml.)	Before test dose	25	30	25
	1 hour after ..	190	65	25
	3 hours after ..	345	385	25
	24 hours after ..	..	45	..

The gastric juice before histamine contained no free HCl and 1 ml. total acid per litre. 20, 40, and 60 minutes after histamine free HCl was 3·5 ml., 4·3 ml., and 3·6 ml., and total acidity 5·8 ml., 6·5 ml., and 5·8 ml. per litre gastric juice. Repeated examinations of the fæces for occult blood were negative.

TABLE II—IRON ABSORPTION AFTER FERRIC CHLORIDE COMBINED WITH ASCORBIC ACID, NORMAL GASTRIC JUICE, AND INTRINSIC FACTOR BY MOUTH

Tests 4–7		4. Ferric chloride with 500 mg. ascorbic acid	5. Ferric chloride with 1000 μg. cyanocobalamine	6. Ferric chloride with normal gastric juice	7. Ferric chloride with intrinsic factor (8 tablets bendogen) *
Serum-iron (μg. per 100 ml.)	Before test dose	50	35	35	40
	1 hour after ..	260	105	..	145
	3 hours after ..	390	60	120	..
	6 hours after ..	350	35†	..	..
	24 hours after..	..	..	..	30

* Each bendogen tablet contains 280 mg. intrinsic factor + 60 μg. cyanocobalamine.

† 6½ hours after test dose.

X-ray and Endoscopic Findings

The anteroposterior chest X-ray picture showed an opacity to the right and overlapping the cardiac shadow. In the oblique position a triangular cavity, 5 cm. high and 3 cm. wide, with a fluid level, could be seen in the posterior mediastinum. The base of the cavity was 1 cm. above the diaphragm: its apex was continuous with the band-like shadow of the œsophagus. The barium meal showed it to be the fundus of the stomach (fig. 1); and in the Trendelenburg position the whole fundus could be made to slide into the chest.

On œsophagoscopy the intrathoracic part of the stomach appeared normal.

Operation and Progress

At operation the œsophageal hiatus was dilated, permitting the passage of the stomach through it. The defect was repaired following Allison's technique (Allison 1951). Postoperative recovery and progress was satisfactory. The anæmia disappeared.

TABLE III—ABSORPTION OF FERRIC CHLORIDE AFTER A SEVEN-DAY COURSE WITH BENDOGEN

Test 8	Serum-iron (μg. per 100 ml.)
Before test dose	80
1 hour after	105
6 hours after	100

Investigation of the Anæmia

A series of tests were performed before the operation. Table I (tests 1–3) shows that bivalent iron was eagerly absorbed in the form of both gluconate and sulphate but that there was no absorption of trivalent iron.

Test 3 was repeated on a patient with Banti's syndrome who had developed posthæmorrhagic anæmia. His serum-iron before the test was 60 μg. per 100 ml. An hour after the test dose (containing 176 mg. Fe^{+++}) it was 75 μg., and two hours later 95 μg. per 100 ml. One may conclude that the ferric iron was converted to ferrous iron by a reducing agent in the stomach: ferric chloride is difficult to absorb since it combines with gastric mucus.

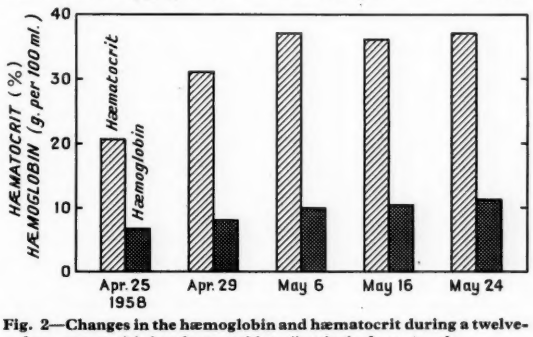

Fig. 2—Changes in the hæmoglobin and hæmatocrit during a twelve-day course with bendogen tablets (intrinsic factor) only.

Table II (tests 4–7) shows the effect of combining the dose of ferric chloride with the administration of ascorbic acid, normal gastric juice, cyanocobalamine (vitamin B_{12}), and Castle's intrinsic factor. All three facilitated the absorption of iron. The iron-absorption two days after a seven-day course of 'Bendogen' (intrinsic factor), 4 tablets daily, is shown in table III. The findings suggest that stored intrinsic factor can act as a reducing agent in the stomach.

The hæmopoietic activity of intrinsic factor was shown in our patient by a rise in his hæmoglobin level from 6·6 to 10 g. per 100 ml. and by the rise in his hæmatocrit

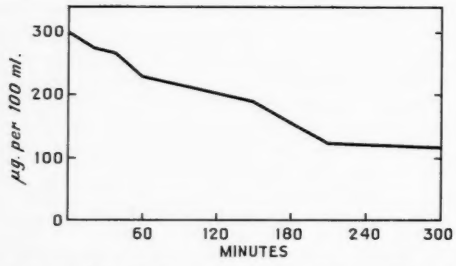

Fig. 3—Serum-iron discharge curve after 12·5 mg. Fe^{++} intravenously.

from 20·5 to 37% (fig. 2). Within twelve days of starting him on intrinsic factor treatment he improved considerably, whereas previous intensive courses of oral and parenteral iron had been ineffective or only slightly effective.

After completion of the tests shown in tables I–III, an inorganic ferrous preparation was given intravenously to show the rate at which iron was taken up from the blood (fig. 3).

Discussion

The iron in food is in the form of polymolecular compounds. These are broken down in the stomach to trivalent iron ions; and these, in turn, are reduced to bivalent ions. The first of these two changes depends on the presence of hydrochloric acid in the stomach while the second can take place through the intervention not only of exogenous but also of endogenous reducing agents. Our tests show that normal gastric juice contains such a reducing substance; and test 8 suggests that this may be Castle's intrinsic factor. It is possible, of course, that other endogenous reducing substances also exist.

Several observations support the view that there is a qualitative or quantitative intrinsic-factor defect in the anæmia of the hiatus hernia. Anæmia complicates almost exclusively those cases in which the fundus and part of the body of the stomach is herniated into the chest (Murphy and Hay 1943, Wintrobe 1947); and in man these are the regions where intrinsic factor is secreted (Girdwood 1957). The administration of intrinsic factor, moreover, quickly corrects the anæmia—as does successful operative repair.

Test 4 (table II) points to a possible parallelism between the action of ascorbic acid and of intrinsic factor. In our patient food iron should have been transformed into trivalent iron by his normal hydrochloric acid; and, since trivalent ions can be reduced by ingested ascorbic acid, no anæmia should have developed in him while he was receiving ascorbic acid. Since he did, however, develop anæmia, we are forced to conclude that hydrochloric acid does not complete the transformation of food iron to trivalent ions or that it cannot do so without intrinsic factor.

At a later date a repeat absorption test of ferric chloride showed partial absorption; but, since effective iron administration is known to improve gastric function (Lyngar 1950), this does not invalidate our conclusions.

Summary and Conclusions

Bleeding, achlorhydria, and chronic œsophagitis cannot be held responsible for every case of anæmia that complicates hiatus hernia.

It seems that the chief cause of this type of anæmia is deficiency of a gastric factor which reduces trivalent Fe^{+++} to bivalent Fe^{++} ions. In these patients the trivalent iron is neither absorbed nor reduced.

In a case here reported the simultaneus administration of normal gastric juice assured the absorption of iron given in trivalent form. A series of tests led us to conclude that the main endogenous reducing substance in normal gastric juice is Castle's intrinsic factor.

We are indebted to Prof. A. Gouttas, director of the clinic, for permission to publish this case. We also wish to thank Mr. K. Gad Andresen, director of the pharmaceutical firm G.E.A. Ltd., of Copenhagen, Denmark, who have supplied the 'Bendogen' for our experiments.

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Medical Societies

MANCHESTER MEDICAL SOCIETY

Halothane and Autonomic Nervous Activity

Prof. W. D. M. PATON, speaking to the section of anæsthetics on Feb. 19, said that one of the most interesting properties of halothane is the hypotension it can induce. In investigating this, some of its other actions deserve attention; thus the low water solubility combined with a high fat solubility means that, although recovery may be rapid and complete with short exposures, long exposures to halothane may be followed by a rapid partial recovery and a much slower period of return to full normality. The depressant action on respiratory minute volume and response to CO_2 shows that halothane can depress the respiratory centre. The action on the neuromuscular junction, potentiating block by *d*-tubocurarine but not itself producing block, shows its action at one cholinergic synapse.

The hypotension produced is accompanied, in man, by a striking bradycardia. Although this resembles the action of veratrine, the other features of halothane exclude a mechanism of this type. Since it does not reduce the action of directly acting vasoconstrictors, it is not an anti-adrenaline, and its direct relaxant effect on smooth muscle can only be slight. The possibilities remain that it blocks ganglia or that it depresses vasomotor activity centrally. Halothane can block all ganglia tested, if given in sufficient concentration; but at concentrations up to 2% large falls of blood-pressure occur unaccompanied by block of superior cervical or vagal ganglia; salivary secretion to chorda-tympani stimulation, however, is readily reduced. Ganglion block, if present, must therefore be intensely and uniquely selective. Since neither evisceration nor splanchnic-nerve section produce such a hypotension or prevent it, it is difficult to assume that a selective action on splanchnic ganglia is a sufficient cause for the hypotension.

On the other hand, halothane has a number of central actions not displayed by all anæsthetics. The knee-jerk is reduced by low concentrations. The pressor response to spinal-cord excitation can be greatly diminished. Reflex activation (through a vagosympathetic anastomosis) of the superior cervical ganglion is more readily blocked than preganglionic trunk stimulation. The pressor response to stimulating the central end of the cut splanchnic nerve is reduced much more readily than that to excitation of the peripheral end.

Professor Paton concluded that halothane is an anæsthetic with distinctly individual features, of which a low water solubility, high fat solubility, and an unusual preference for central depression of autonomic activity are especially interesting. The bradycardia in man still requires analysis. The

properties of halothane suggest that it should be considered not merely as an alternative to other anæsthetics but as potentially offering special advantages in particular circumstances.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE

Liver Disease in the West Indies

AT a meeting on Feb. 19, Prof. K. R. HILL commented on the relative infrequency of cirrhosis of the liver and of primary hepatic carcinoma in the West Indies.

Hepatic veno-occlusive disease was found predominantly in children aged 1–5 years; the children were all significantly underweight and had a background of malnutrition. The essential finding in the acute stage of the disease was blockage of the medium-size and smaller hepatic veins by subendothelial swelling of the intimal tissues; this swelling was apparently due to œdema but later became collagenous. The intimal occlusion produced a centrilobular block with distension of the tributary sinusoids. The condition was thought to be caused by the ingestion of " bush teas " or other food containing the pyrrolizidine group of alkaloids found in the plants of genus *Senecio* and *Crotalaria*. Recently Dr. C. F. Stephenson, in Professor Hill's laboratory at the Royal Free Hospital, had produced veno-occlusive disease in rats by the intraperitoneal injection of monocrotaline, isolated from several species of crotalaria.

With regard to the vomiting sickness of Jamaica, Professor Hill stated that at postmortem examination there invariably were fatty metamorphosis of the liver and fatty changes in other organs such as the kidney and heart. Hypoglycæmia had been recognised as an invariable accompaniment of the sickness; and work in Jamaica had indicated that the vomiting was relieved and the patient's condition dramatically improved by intravenous administration of glucose. Recent work in Jamaica strongly supported the conclusion, earlier reached by Sir Harold Scott, that consumption of unripe ackees was the cause of vomiting sickness. Prof. C. H. Hassall, then of the Department of Chemistry in the University College of the West Indies, had isolated from ackees two compounds named hypoglycin A and B, and it had been shown that in animals severe hypoglycæmia, depletion of liver glycogen, and death resulted from administration of these substances.

Dr. KATERINA RHODES, opening the discussion, said that veno-occlusive disease was unknown in the well fed, and that in patients with this disease there was invariably a history of protein deficiency. In Jamaica most mothers worked to support their family, and infants at the age of 3–4 months were weaned and placed on a diet consisting of cornmeal porridge, condensed milk, and " bush tea."

HEBERDEN SOCIETY

THE society met in London on Feb. 27.

Ankylosing Spondylitis ?

Dr. R. M. MASON described the case of a young man who had been invalided out of the Forces because of gout. X-rays showed both cystic and " rheumatoid " destructive erosions of the toes, and there was a history of gonorrhœa with achilles bursitis. The Rose test was negative, the plasma-uric-acid estimations were marginally increased, and the sacroiliac joints were normal. Reiter's disease was considered likely. Later two cousins were found to have typical ankylosing spondylitis, and other relatives had symptoms which might suggest this. Since ankylosing spondylitis is often familial it seemed possible that the original patient may have had a form of ankylosing spondylitis with involvement of peripheral joints but not of central joints.

Rupture of Extensor Tendons

Mr. O. J. VAUGHAN-JACKSON described attrition rupture of the extensor tendons in rheumatoid arthritis. The little-finger tendon was the first to go, and the other tendons then ruptured seriatim—ring, middle, index, in that order. Prompt exploration always revealed a hole in the distal tendon compartment over the lower end of the ulna through which a bony spicule abraded the tendon. Sometimes the tendon ends were joined by a thin tube of peritenon within which the severed ends had retracted. Removal of the lower end of the ulna and grafting the tendons restored normal function. Flexor tendons might rupture similarly. Tendon ruptures caused more deformity than had hitherto been recognised and were unusual among rheumatoid lesions in being repairable.

Sanatorium Regime

Dr. W. E. WENLEY said that 40 patients with severe and long-standing rheumatoid arthritis had been treated for an average of six and a half months with prolonged bed rest, out of doors as much as possible, and with suitable splinting. Other treatments had been much restricted. By the time of discharge the proportion only partially disabled had increased from 50% to 68% and the completely incapacitated group had decreased from 50% to 24%. Further improvement had been observed after discharge. Severe incapacity appeared to be no contraindication to admission to a sanatorium regime.

Dr. J. J. R. DUTHIE reported that he had used complete body splintage for up to a month in patients with rheumatoid arthritis. Ankylosis did not occur and the disease was considerably improved.

Arthritis, Genital Infection, and Uveitis

Dr. R. D. CATTERALL had studied the association of arthritis and non-specific genital infection in male patients with uveitis at the Institute of Ophthalmology. Of 222 patients, 142 were found to have chronic prostatitis, diagnosed by the finding in the prostatic fluid of clumps of pus or of more than 10 white blood-cells per high-power field. If only cases with anterior or generalised uveitis were included, the prevalence of prostatitis was about 75%. In contrast, prostatitis was found in only 29% of 44 controls taken from the surgical wards. Reiter's disease (diagnosed in 52 patients), ankylosing spondylitis (in 29 patients), atypical sacroiliitis (in 14 patients), and plantar fasciitis (in 7 patients) might be manifestations of one disease which was caused by or associated with genital infection and of which anterior uveitis was a common component.

The Kidney in Gout

Dr. D. GREENBAUM had studied renal function and renal biopsies in 13 patients with gout, 3 of whom had obvious renal disease with uræmia. Of the remaining 10, who appeared to be healthy apart from their gout, 8 had moderately abnormal renal function tests and 8 had an abnormality of the renal biopsy specimen consisting in slight increase in interstitial fibrous tissue only. Uric acid or urates could not be demonstrated in the biopsy specimens. Of a further 8 kidneys from gouty patients examined post mortem, 7 of which were histologically abnormal, uric acid was found in only 2. Renal biopsy in these patients had not thrown any further light on renal damage in gout, although completely normal kidneys, according to histological appearance and function tests, were not found in any of the patients.

Rose-Waaler and Latex-fixation Tests

Dr. V. L. STEINBERG had compared the Ball [1] modification of the Rose-Waaler test and the Singer and Plotz [2] latex-fixation test in 504 patients. Of 259 with rheumatoid arthritis, defined by accepted criteria,[3] both tests were positive in 153; 15 patients were Rose-positive and latex-negative; 10 were latex-positive and Rose-negative; and in 81 both tests were negative. Of 245 patients with miscellaneous conditions, both tests were negative in 230; 5 patients were Rose-positive and latex-negative; 6 were latex-positive and Rose-negative; and both tests were positive in 4. The less time-consuming latex test was preferable for routine clinical use.

1. Ball, J. *Lancet*, 1950, ii, 520.
2. Singer, J. M., Plotz, C. M. *Amer. J. Med.* 1956, **21**, 888.
3. Ropes, M. W., Bennet, G. A., Cobb, S., Jacox, R., Jessar, R. A. *Bull. rheum. Dis.* 1956, **7**, 121.

New Inventions

APPARATUS FOR MAINTAINING STERILITY OF CHEATLE FORCEPS

THE instrument described here originated from an inquiry from the hospital house committee regarding an increase in the cost and amount of alcohol supplied to the operating-theatre. This alcohol was used in metal jugs which held the Cheatle forceps used for handling instruments and laying trolleys.

Our first approach was to suggest that the forceps be immersed in some other type of fluid. The objection here was that any fluid used was liable to run down the handles of the forceps on to the hands of the nurses handling the instruments. The other difficulty was that the tops of the cans holding the Cheatle forceps could not be maintained in anything approaching a sterile condition.

For that reason a heat-sterile holding mechanism was planned, and experiments were carried out to determine the

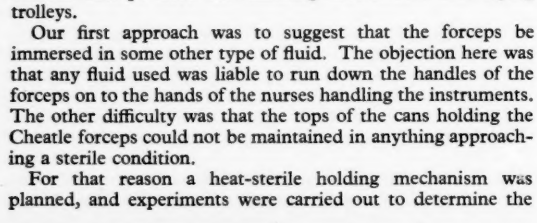

Fig. 1.—Instrument in use in the operating-theatre anteroom.

temperature at which the handles of the forceps became too hot to hold, and the highest temperature at which the working length of the forceps could be maintained without the handles becoming too hot. It was found that, with the mouth and gripping parts of the forceps maintained at approximately 130°C, the handles outside the heating area could be held conveniently.

Accordingly a form of dry heating was devised using pipe steam as the source of heat (electricity could be used as an

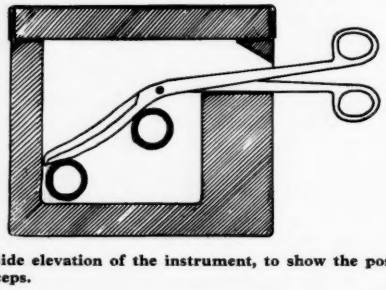

Fig. 2.—Side elevation of the instrument, to show the position of the forceps.

alternative). The apparatus is illustrated in figs. 1 and 2. It consists of a main outer case of 18-gauge stainless steel with joints welded and glazed off, lined by 1-in. thick fibre-glass, matt, with a double layer beneath the anterior shelf.

The heating element consists of 1-in. B.S.P. copper, two rounds, with inlet and outlet the same end, fitted with a control valve on the inlet and a ' Spirax ' 9/200 trap, strainer, and sight-glass on the outlet. The steam-pressure is 60 lb. per sq. in., so that the temperature of the copper pipes is approximately 150°C. The case measures $24 \times 7^1/_4 \times 8^1/_4$ in., and is made to hold 12 Cheatle forceps.

Bacteriological tests were carried out on various organisms inoculated on to discs of filterpaper enclosed in small paper envelopes. These were heated in the oven, clipped in Cheatle forceps in a position midway between the two heating pipes. Staphylococci, streptococci, and *Escherichia coli* were killed in 5–30 minutes, and spores of *Bacillus subtilis* in 4 hours.

The outside face of the container, with the holes through which the Cheatle forceps pass, has been bacteriologically examined on many occasions, and this area appears to be maintained in a sterile condition. The air-temperature inside the case is approximately 125°C.

This instrument has now been in routine use in the hospital theatre for approximately two years, and is much preferred by the nursing staff to the conventional jug of antiseptic. The theatre routine is as follows:

The forceps are all heat-sterilised in the morning and placed in the container thereafter. If the forceps come into contact with non-sterile material in use, or fall on the floor, they are not returned to this container without having previously been passed through a sterilising process.

We have attempted to culture organisms from forceps used in this way on many occasions, and have never succeeded in growing organisms from them.

The initial cost of making this instrument was £17, and the thermal consumption appears to be in the region of 450 watts. The operational cost works out at about 2*s*. a week. This device saves money, and is more effective than the conventional " Cheatle pot ".

Constructional plans, made by Mr. R. Swinden, the hospital engineer, are available to anyone interested.

JOHN L. EMERY
M.D. Brist.
Consultant pathologist
W. F. ALSOP
F.I.M.L.T.
Chief technician

Department of Pathology,
Children's Hospital,
Sheffield, 10

A BURETTE FOR INTRAVENOUS INFUSION IN INFANTS

WHEN operating on newborn infants for urgent congenital malformations, accurate replacement of fluids and salts by intravenous infusion and transfusion is of great importance. Most of these infants require only very small quantities of fluids, and intravenous infusions running at 5–10 ml. per hour are commonly used. With the infusion bottles used in this country it is impossible to measure such small quantities accurately.

In our neonatal surgical unit, for over 3 years, we have used a simple glass burette connected between the drip bottle and the drip chamber. This has been very satisfactory.

The burette is a modification of one originally devised by Dr. T. E. D. Beavan, of Chester. It is 10 in. long and can therefore be packed into a small container for sterilisation. Because it is graduated in millimetres, quantities of fluid down to 0·25 ml. can easily be estimated. Its total capacity is 30 ml., but at the slow infusion-rates used only infrequent refilling is needed.

As can be seen from the figure, rubber corks with a central hole for a glass tube are inserted into each end of the burette and connected up with an ordinary drip set in such a way that there is a length of tubing, controlled by a clip, between the drip bottle and the top of the burette. The lower end of the burette is connected directly to the drip chamber. The infusion apparatus is therefore a little longer than the standard set and has to be suspended higher. The side-arm of the burette which allows air to enter should be lightly plugged with a piece of cotton wool.

The burette is manufactured for us by Mr. J. W. Turner, 13, Derby Lane, Liverpool, 13.

P. P. RICKHAM
M.S. Lond., F.R.C.S., D.C.H.
Consultant Pædiatrician

Alder Hey Children's Hospital,
Liverpool, 12

Reviews of Books

Recent Studies in Epidemiology

Editors: J. PEMBERTON, M.D., M.R.C.P., D.P.H., professor of social and preventive medicine, Queen's University, Belfast; H. WILLARD, M.D., coordinator of rehabilitation, Cornell University Medical College. Oxford: Blackwell Scientific Publications. 1958. Pp. 203. 25*s*.

IN certain circles epidemiology is now all the go. This renaissance comes from realisation that the objective study of numerical data, from which so much was learnt about the communicable fevers, is equally fruitful when applied to the investigation of diseases which are not infectious. The art of epidemiology lies in framing exact and answerable questions rather than in collecting answers. The raw material may be existing statistics from departments of the Government or from hospitals or health authorities. Most of these have the disadvantage that the figures have not been collected with the investigator's end in view and may therefore be incomplete, but on the other hand bias in their collection is unlikely. Some such investigations have been most fruitful—for example, D. D. Reid's use of the sickness records of the Post Office in relation to chronic bronchitis. The survey in which the questions are set and the data then collected independently is both more ambitious and more expensive. In the U.S.A. much attention has been paid to numerical methods of assessing the value of community health services. It would be interesting to see these methods applied to some of the larger health authorities in Great Britain: there is a good deal of dead wood in public health, and the ratepayers might soon find that the expense of the investigation was justified. Epidemiology in general practice owes a great deal to W. N. Pickles; and his standard has been followed by the College of General Practitioners.

This book is the product of a colloquy held in Holland in 1957. The contributors came from the U.S.A., Sweden, Norway, Czechoslovakia, Canada, Holland, and Great Britain, and each had something of value to say. Careful reading will give anyone a good idea of the aims, methods, rewards, and pitfalls of epidemiology.

The Neurologic Examination

2nd ed. R.N. DEJONG, M.D., professor of neurology and chairman of department of neurology, University of Michigan Medical School. London: Pitman Medical Publishing Co. 1958. Pp. 1078. 140*s*.

THIS book covers a larger field than its title suggests. The author rightly wishes to present normal as well as abnormal aspects of the neurological examination, and he gives concise but informative summaries of the anatomy and physiology of each region. In dealing with abnormal physical findings he also gives an outline of the diseases in which they are likely to be found. There is a particularly useful section on methods of distinguishing organic disease from hysteria and malingering. The book deals only with clinical neurological examination and examination of the cerebrospinal fluid, and does not extend to electroencephalography and radiographic examination.

Disinfection and Sterilization

G. SYKES, M.SC., F.R.I.C. London: E. & F. N. Spon. 1958. Pp. 396. 75*s*.

MANY hospitals may soon accept the advice of the Nuffield Provincial Hospitals Trust and appoint someone to supervise sterilisation and disinfection. These duties cannot be properly performed by simply memorising approved methods. The choice and control of methods should depend on local circumstances and be based on sound knowledge of the principles of disinfection. In this book these principles are authoritatively described. The chapter on steam sterilisation, unlike some other such accounts, can be understood by an ordinary human being. This work is up to date and includes methods still under investigation, such as the use of iodophores, ethylene oxide, and the various forms of radiation.

Hématologie clinique

JEAN BERNARD, professor in the Faculty of Medicine, Paris; MARCEL BESSIS, director of the research laboratory of the National Blood Transfusion Centre, Paris. Paris: Masson. 1958. Pp. 526. Fr. 14,500.

THE outstanding feature of this bulky volume is the illustrations. The colour plates are photomicrographs, and the reproduction is remarkably clear; nuclear detail has nearly always been successfully reproduced, and so has the detail of nucleoli and cytoplasmic granulation. The plates show typical fields from almost every recognised blood disease, and pictures of Reed-Sternberg cells seen in material from lymph-gland puncture in Hodgkin's disease are specially interesting. The other pictures are equally well reproduced. In addition to the named authors, 16 French hæmatologists collaborated in preparing this book. Most of it was designed in the first place for an exhibit at the 5th International Congress of Hæmatology. Unfortunately much of the material seems to have been put in directly from the exhibits, and consequently the text is excessively tabulated. The treatment of blood diseases is dealt with in very cavalier fashion; graphs showing the progress of individual patients are no substitute for proper consideration of dosage and of how to control the various forms of treatment.

English, American, and German publishers are tending to segregate elaborate illustrations into properly designed atlases. The cost of comprehensive works such as this one from France virtually precludes personal ownership; and the size is often such that, after an admiring glance through, the volume is heaved on to the library shelf—to gather dust.

A Bibliography of Internal Medicine

Communicable Diseases. ARTHUR L. BLOOMFIELD, M.D., professor emeritus of medicine, Stanford University. Chicago: University of Chicago Press. London: Cambridge University Press. 1958. Pp. 560. 75*s*.

THE surge of new knowledge in medicine has created a tremendous problem. Professor Bloomfield believes that the modern student tends to keep up on the new, the esoteric, and the curious at the expense of the fundamental and the historical. In current medical writing what is referred to as the older literature often turns out to be from the previous decade. Few medical students remember Banting, Minot, or Lewis. One in an examination stated that the malarial parasite was discovered by Vivax.

The author has set out to provide a selected bibliography of important contributions in the 19th and 20th centuries with critical comments that might stimulate further reading. The present volume, concerned with thirty communicable diseases, is a valuable source book; the longest section concerns tuberculosis. There is also a short historical preface to most of the sections and an index to each.

Ward 4

The Mallinckrodt Research Ward of the Massachusetts General Hospital. JAMES HOWARD MEANS. Harvard: Cambridge University Press. London: Oxford University Press. 1958. Pp. 187. 36*s*.

Dr. J. H. Means, recently Jackson professor of medicine at Harvard, has taken a prominent part in organising medical research, and in this book he describes a successful enterprise. Ward 4, with its 10 beds and adjacent research laboratories, was opened in 1925 at the Massachusetts General Hospital with the object of carrying out basic and applied research. No fees were charged, and the full cooperation of the patients in the investigations was particularly sought. Most of the chapters describe simply the investigations carried out in the ward; and with the help of the glossary the layman should easily follow even complex topics. Means divides research, basic or applied, into three groups: (1) method-centred ("here is an instrument or method—what is it good for?"); (2) object-centred or categorical ("here is a problem—how shall we solve it?"); (3) free research ("here is a worker of high

promise—let's give him every opportunity to make the optimum use of his talents"). "Free research" is in danger of being starved; and throughout the book we are persuasively shown how it can be fostered and made to flourish.

Convulsive Disorders of Children

DORA HSI-CHIH CHAO, M.D., physician and assistant director, Blue Bird Clinic; RALPH DRUCKMAN, M.D., neurologist, Blue Bird Clinic; PETER KELLAWAY, A.M., PH.D., director, Blue Bird Clinic; Baylor University College of Medicine, Houston. Philadelphia and London: W. B. Saunders. 1958. Pp. 151. 42*s*.

THIS short book is a ward handbook rather than a comprehensive guide. After an introduction to the physiological background of seizures, a discussion on symptomatic epilepsy follows logically, since focal epilepsy (par excellence symptomatic) can be used to illustrate abnormal neuronal discharge of localised areas of brain. Idiopathic or genetic epilepsy is still regarded as an entity by these authors; and they consider petit mal, akinetic attacks, myoclonic jerks (so-called "petit-mal triad"), and grand mal as all at times belonging to it. Benign febrile convulsions are classed as non-epileptic, mainly because the majority of affected children are not subject to fits later. This is the view held by most pædiatricians, though it is difficult to see why the physiological upset of fever should be segregated from other factors, such as teething and gastrointestinal upsets, also known to precipitate convulsions occasionally. In all such cases the soil is probably as important as the seed. A similar argument applies in lesser degree to breath-holding attacks, which also are regarded here as non-epileptic. Treatment is not well covered, though surgical treatment is seen in sensible perspective. The book has a separate and useful section on electroencephalography in the diagnosis of seizures. It would be of value in a children's ward for the junior intern, though inadequate for a neurological unit.

Radioactive Isotopes in Clinical Practice

EDITH H. QUIMBY, professor of radiology, College of Physicians and Surgeons, Columbia University, New York; SERGEI FEITELBERG, director, physics department, Mount Sinai Hospital; SOLOMON SILVER, attending physician, chief thyroid clinic, Mount Sinai Hospital. London: Henry Kimpton. 1958. Pp. 451. 75*s*.

THIS book is based on a course of lectures given at Columbia University. It is in three parts. The first gives a very good account of the basic physics necessary to understand the nature of radioisotopes and the methods of measuring them. The second is on instrumentation and laboratory methods; this is rather diffuse and contains some sections which seem irrelevant to the main theme. The third, on clinical applications, is rather disappointing. The value of this work, though it contains much useful information, would be increased for clinical workers if the first and second sections were somewhat shorter and the third expanded. It is disappointing to find so much about the thyroid and ^{131}I but no mention of the light thrown on the blood-electrolytes by studies with ^{24}Na and ^{42}K, or of the important studies on the plasma-proteins using ^{131}I-labelled human serum-albumin. The therapeutic applications are very much in the hands of specialists in this country; and the book seems to contain too little for them, but too much for the general reader.

Biographical Memoirs of Fellows of the Royal Society

Vol. 4. London: Royal Society. 1958. Pp. 359. 30*s*.

THE latest addition to this series of admirable biographical studies contains eight of special interest to medical readers.

Walter Elliot is best known as a politician, particularly from his connection with the active and progressive Empire Marketing Board. "No one contributed more to the creation of that initiative and the generation of that enthusiasm than Walter Elliot. He brought to its research activities not only a scientific training but ideas and zest and gaiety. His mind, especially when refreshed by one of his frequent visits to Scotland and communings with John Orr, then Director of the Rowett Research Institute, bubbled over with ideas."

A. J. Ewins, E. L. Kennaway, J. B. Leathes, and Heinrich Wieland represent biochemistry with great credit. Graham Kerr was a zoologist who wrote a textbook for medical students. He was a keen teacher with much excellent research work to his credit. "In the department, when not lecturing or demonstrating, he used to work behind a locked door, and at a knock this barrier would be opened only a few inches and a somewhat ferocious face would appear in the chink to see who was there. If admitted, the visitor would be welcomed with a charming old-world courtesy which all his friends will remember with affection." J. H. Parsons, the ophthalmologist, held a unique position in that specialty. Early in the 20th century he grasped the significance of the changes that were at that time becoming apparent in the progress of medicine. To a generation which hardly understood, he preached that advances in the treatment of cataract would come, not from elaborating operative techniques but from understanding the biochemistry of the lens and its respiratory mechanism; and in the treatment of glaucoma from elucidating the dynamics of the aqueous humour. Charles Todd did much original bacteriological research, first in the Serum Institute in Cairo and later at the National Institute for Medical Research at Hampstead.

This book should find a place in every medical and scientific library of standing.

Textbook of Physiology and Biochemistry (4th ed. Edinburgh: E. & S. Livingstone. 1959. Pp. 1065. 65*s*.).—The authors of this successful work—Prof. G. H. Bell, Prof. J. N. Davidson, and Prof. Harold Scarborough—stress that it is meant to be, not a full reference volume, but an introduction to physiology, and in 1020 pages it covers well such biochemistry and physiology as are needed by medical students in their preclinical years. At the end of each chapter a few well-selected references enable the student to discover more about chosen aspects. As in previous editions good diagrams and interesting photographs are a special feature of this work, which may be warmly recommended to students and to those postgraduates who want a balanced and up-to-date account of physiology and biochemistry from which they can proceed to more detailed knowledge.

Health in Industry (London: Penguin Books. 1959. Pp. 288. 4*s*.).—The writing of a "Penguin" on industrial medicine must have been a forbidding task, but Dr. Donald Hunter has clearly found it well within his compass. He provides a wealth of information from accounts of occupational diseases of ancient times to the development of modern thought on preventive medicine in industry, and finally to present-day techniques in handling radioactive materials. The style of writing is free-and-easy with a dash of humour—sometimes a little sardonic. The chapters on factory legislation, accidents, and dust diseases are outstanding in their clarity, but the whole book is of a high standard. Lay readers will find the glossary of technical terms useful, and there is a list of references for additional reading. The index is good. This book might be read with profit by all who practise medicine, and it could become a "must" for medical students.

The Sella in Health and Disease (*British Journal of Radiology*, 1958, suppl. 8. Pp. 100. 35*s*.).—To the clinical radiologist the most important part of this well-written monograph by Dr. Mahmoud El Sayed Mahmoud is an analysis of the type and frequency of changes produced in the sella turcica by tumours at various sites in the skull. The author found that when the lesion lay within the pituitary fossa this was enlarged from within in 98% of cases. Eosinophil adenoma did not cause greater enlargement than the chromophobe type. In the suprasellar group of tumours craniopharyngiomas produced changes four times as frequently as either suprasellar meningiomas or gliomas; the commonest changes were widening of the sellar outlet due to backward deflection of the dorsum sellæ and destruction of the posterior clinoids. The incidence of damage to the sella was found to be higher with infratentorial than with supratentorial tumours.

THE LANCET

LONDON 14 MARCH 1959

Gastrointestinal Hæmorrhage

GASTROINTESTINAL bleeding from duodenal or gastric ulcers, and sometimes from acute erosive gastritis, remains one of the commonest emergencies in patients admitted to hospital. In young people the mortality is low, although the patients may remain in hospital for several weeks. But in older people, particularly those over 70 years of age, it is a very serious condition with a high mortality; and there is evidence that an increasing proportion of those admitted are elderly.[1]

The doctor's first duty is to decide at once how ill the patient is. An estimate must be made of the extent of blood-loss and its effect. And here we run into difficulties. First, only rarely is the patient's hæmoglobin level before the onset of hæmorrhage known; often it was reduced. Secondly, from the moment of hæmorrhage water passes from the extracellular spaces into the blood, progressively diluting the remaining red blood-cells. For these reasons estimates of the hæmoglobin level or hæmatocrit may be misleading, and result in considerable underestimates of the extent of blood-loss. Accordingly, clinicians have been more concerned with the effects of the bleeding, judged by the blood-pressure and the pulse, than with any laboratory measurements; and in general the more rapid the pulse and the lower the blood-pressure the worse is the patient's condition. But there are exceptions, and everyone remembers patients who did badly when all the signs pointed to only minor bleeding. In view of these difficulties a report by TUDHOPE [2] on the loss and replacement of red blood-cells in gastrointestinal hæmorrhage is particularly valuable.

He describes a technique using ^{51}Cr-labelled red blood-cells in which a known quantity of cells of known activity was infused after hæmorrhage, and the total red-cell volume was calculated from its dilution. A second measurement was made several months later, when the red-cell volume was assumed to have returned to normal, and the percentage red-cell loss in the acute episode was calculated retrospectively. TUDHOPE studied 30 patients after gastrointestinal hæmorrhage, and related the percentage red-cell loss to the subsequent pulse-rate and blood-pressure. He confirms that a systolic pressure of less than 110 mm. Hg and a pulse-rate of more than 110 per minute are associated with severe blood-loss—usually more than 50% of the total red-cell volume. But in a few cases severe blood-loss was associated with little change in the pulse-rate or blood-pressure; and it is in such cases that the new technique is likely to be of great value. Two other points emerge from this part of TUDHOPE's report: in 18 of the 30 patients more than 50% of the red-cell volume was lost by the time the observations were made; and, in general, bleeding was more severe in older patients.

It should not be assumed that these findings are a warrant for immediate transfusion of very large amounts of blood. The mortality in young people after gastrointestinal hæmorrhage is low, and the risks of transfusion are not inconsiderable. No patients die immediately from anæmia: they die from a decreased effective circulatory volume. Thus, if infusion is deemed urgent, innocuous plasma-expanders should be given until properly matched whole blood is available. Even then very large transfusions should be avoided if possible. KREVANS and JACKSON [3] have shown that massive blood-transfusions are sometimes followed by a sharp fall in the platelet-count, and bleeding is thereby prolonged. Two, or at the most three, pints of blood should be given initially, and morphine injected intramuscularly. It has been said that morphine may cause vomiting and so prolong bleeding, and that heroin is to be preferred; but in practice small doses of morphine are extremely satisfactory. If bleeding continues—which is particularly likely in the elderly patient—then surgical advice should be sought at once. Not all patients need an operation at this stage, but treatment is best decided by consultation. In most cases, with this treatment bleeding will stop and the circulatory volume and extracellular fluid will revert to normal. But the patient will be left with a low hæmoglobin level, and replacement of red cells from the bone-marrow is a slow business. It is a natural temptation to hasten progress by a further blood-transfusion; but this is probably unwise and usually unnecessary. Leaving aside the intrinsic dangers of transfusion, there is always the chance of renewed hæmorrhage due to too rapid infusion; and furthermore TUDHOPE has clearly shown that transfusion at this time interrupts the normal marrow action of replacing red cells.

By TUDHOPE's technique continued bleeding of small degree is easily detectable from the presence of radioactivity in the fæces. This is obviously a far more satisfactory method than chemical testing for breakdown products of hæmoglobin; indeed, by any earlier method it is difficult to establish without long-continued observation that bleeding is continuing. There is much to be said for making this technique available in all hospitals which admit many patients with hæmorrhage.

The Hazard of Water Enemas

ENEMAS have been used for well over 2000 years [4]; but surprisingly little is known about the most desirable forms of enema solution and the precise indications for their use. Of the watery evacuant enemas, probably the most usual are either tap-water alone or tap-water

1. Avery Jones, F. Modern Trends in Gastro-enterology; p. 432. London, 1952.
2. Tudhope, G. R. *Quart. J. Med.* 1958, **27**, 543.
3. Krevans, J. R., Jackson, D. P. *J. Amer. med. Ass.* 1955, **159**, 171; see *Lancet*, March 7, 1959, p. 510.
4. Lieberman, W. *Rev. Gastroent.* 1946, **13**, 215.

to which soap has been added. Plain water is as effective as the *enema saponis* and is less irritating to the colonic mucosa.[5 6] A serious danger is associated with the injudicious use of both plain-water and soap-and-water enemas. Each of these fluids is hypotonic to the blood-plasma, and their rapid absorption from the colon into the blood-stream results in acute lowering of the osmolarity (total electrolyte concentration) of the blood —a change that is reflected promptly throughout the body-fluids, causing symptoms of "water intoxication".[7] This was first recognised as a serious hazard of an evacuant enema by HIATT in 1951.[8] Of his 42 patients with megacolon, 25 (60%) gave a history of systemic reactions following a tap-water enema; in 3 the symptoms were severe, and 1 died. Later RICHARDS and HIATT [9] described 9 patients with megacolon who were acutely ill after a tap-water enema; 2 died. Subsequently others have written about this danger [10–14]; but it is unlikely that all cases are reported. In several of the published cases the correct diagnosis was made only in retrospect; and the syndrome should be better known.

Sometimes this disorder follows a barium enema.[10–13] Barium sulphate, being insoluble, does not modify the osmolarity of the tap-water in which it is suspended, and the solution is therefore equivalent to plain water in its osmotic effects. A barium enema is often administered deliberately in such a way as to spread the barium throughout the whole colon, and the water then comes into contact with a large absorbing surface. Absorption of the water is aided by the not inconsiderable hydrostatic pressure with which some of these enemas are administered. A final aggravation may be the subsequent use of a water enema to promote evacuation of the barium.[10 13]

The sequence of events in many of these cases of water intoxication is much the same. The patients are often infants or children with congenital megacolon or chronic constipation of functional origin. The enemas are given in order to cleanse the bowel of fæces, because of obstruction or distension, or to prepare the bowel for proctoscopic, sigmoidoscopic, or radiographic investigation. Commonly the nurse (or mother) is dissatisfied with the result of the first enema and follows this with a second and even a third. This repetition, with the retention of large volumes of water, is particularly dangerous. The symptoms are mostly due to cerebral disorder: there are drowsiness, apathy, weakness, sometimes periods of excitement and delirium, and finally convulsions and coma. The patients appear pale and cold and are bathed in sweat; owing to this appearance their condition has been described as shock-like—which is incorrect because the blood-pressure is not low until they are moribund, and the pulse is not unduly rapid. Disorders of respiration have been noted in nearly all the reported cases; breathing is usually described as laboured, rapid, or irregular. Nausea and vomiting of clear fluid are common, and usually the patient passes much very dilute urine. The diagnosis should be suspected in any patient who has these symptoms after instillation of water into the colon, and it may be confirmed biochemically by finding a reduced plasma-sodium level. This and other forms of water intoxication have been described in our columns by WYNN and ROB,[15] and osmotic disorders of the body-fluids in general, including water intoxication, by WYNN.[16]

Because of the risk, some pædiatricians claim that a tap-water enema should not be used and advocate isotonic saline solution instead.[9 11–13] RICHARDS and HIATT [9] suggest that 7% gelatin be added to the saline solution to reduce absorption further, but this cannot be added to barium sulphate, which it flocculates. Since salt, besides water, is absorbed from the colon a saline enema may give rise to over-hydration, with general or pulmonary œdema as a possible consequence. Because saline, too, is clearly not without risk, ZISKIND and GELLIS,[14] working at the Boston City Hospital, have made some further observations on tap-water enemas. They gave such enemas, equal in volume to 3·5% of the body-weight, to 11 children with normal colons. None of these children showed significant biochemical changes or symptoms thirty to sixty minutes later; but the volume of fluid returned amounted to only 10–50% of the original volume. ZISKIND and GELLIS do not comment further on this point; but surely the crux of the matter is that much of the enema solution is likely to be retained. One case (a girl aged $4^1/_2$ years) described by ZISKIND and GELLIS is particularly informative. Only after a precipitous fall in the plasma-sodium level (of about 10 mEq. per litre) an hour after the enema did questioning of the mother elicit that the patient had chronic constipation. ZISKIND and GELLIS conclude that a single tap-water enema is safe provided that the patient does not have chronic constipation or a condition interfering with water excretion. But constipation is the condition for which enemas are usually prescribed; and their case, where the diagnosis was missed, lends weight to the arguments of those who proscribe tap-water as an enema.

No doubt opinions as to the best enema solution will continue to be divided. Two millennia of practice have failed to settle a question which a few simple observations along the lines of ZISKIND and GELLIS's work would be expected to solve. Meanwhile those who order enemas should see that the patient is not already overloaded with fluid; that there is no reason, metabolic or other, why the patient should not excrete water freely; and finally that the amount of fluid given and returned is properly recorded. The danger of repeated enemas, especially where much of the first has been retained, should be made clear to all.

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6. Page, S. G., Riley, C. R., Haag, H. B. *J. Amer. med. Ass.* 1955, **157**, 1208.
7. Weir, J. F., Larson, E. E., Rowntree, L. G. *Arch. intern. Med.* 1922, **29**, 306.
8. Hiatt, R. B. *Ann. Surg.* 1951, **133**, 313.
9. Richards, M. R., Hiatt, R. B. *Pediatrics*, 1953, **12**, 253.
10. Jolleye, A. *Brit. med. J.* 1952, i, 692.
11. Steinbach, H. L., Rosenberg, R. H., Grossman, M., Nelson, T. L. *Radiology*, 1955, **64**, 45.
12. Hill, L. F. *J. Pediat.* 1954, **45**, 751.
13. Peterson, C. A., Cayler, C. G. *Amer. J. Roentgenol.* 1957, **77**, 69.
14. Ziskind, A., Gellis, S. S. *A.M.A. J. Dis. Child.* 1958, **96**, 699.
15. Wynn, V., Rob, C. G. *Lancet*, 1954, i, 507.
16. Wynn, V. *ibid.* 1957, ii, 1212.

Adrenal Insufficiency in the Newborn

ACUTE adrenal insufficiency in infants may be a result of hæmorrhage,[1] or it may be due to hypoplasia,[2] as in the cases recorded by Dr. R. G. MITCHELL and Dr. K. RHANEY in our last issue. But more commonly it is associated with congenital adrenal hyperplasia. In this condition, which is now attributed to an inborn error of metabolism,[3] the main clinical manifestation is usually virilisation, with "pseudohermaphroditism" in females and macrogenitosomia præcox in males. In a third of all infants with congenital adrenal hyperplasia an electrolyte disturbance develops in which the serum sodium and alkali reserve are low and the serum-potassium is high—changes typical of Addison's disease.[3] In most cases the disease manifests itself within a few days of birth and nearly always within the first two months.[4] The infant refuses feeds, appears apathetic and limp, and soon starts vomiting. Since the vomiting is often projectile and gastric peristalsis can sometimes be seen, it is not surprising that pyloric stenosis has been mistakenly diagnosed and laparotomy performed.[4] Diarrhœa occurs in about a third of the patients, and constipation in fewer. There is failure to thrive, with loss of weight, persistent or recurrent dehydration, and, in about 10% of cases, pigmentation which may be either general or around the genitalia. The most dramatic manifestations are the crises which occur either spontaneously or in association with infection. There is acute circulatory collapse with pallor, peripheral cyanosis, sweating, loss of consciousness, and sometimes convulsions. The infant may die suddenly from cardiac arrest, presumably due to hyperkalæmia. Adrenal insufficiency may be suspected in female pseudohermaphrodites who are failing to thrive or who collapse suddenly; but in males the genital changes do not usually develop until some time after birth and the diagnosis may be much more difficult. The finding of excessive amounts of 17-ketosteroids in the urine establishes the diagnosis; but this investigation is not easily done in an emergency, especially as a twenty-four-hour specimen of urine is required. But serum-electrolyte changes, together with normal or increased urinary chloride in a dehydrated child, strongly indicate adrenal insufficiency.

Congenital adrenal hyperplasia often affects siblings, and in one family three successive infants were affected.[5] WILKINS [6] cites a suggestion that the disorder may be due to a recessive trait which can express itself only in homozygous offspring. In families in which "the salt-losing type" of syndrome has been found, all the affected siblings had the same form of the disease. BONGIOVANNI [3] has shown that the essential chemical lesion in congenital adrenal hyperplasia is a defect of hydroxylation at the C_{21} atom in the final stages of steroid-hormone synthesis. Hydrocortisone is not produced in normal quantities and its precursor, 17-hydroxyprogesterone, accumulates and is excreted in the urine—largely in the form of its breakdown product, pregnanetriol. The normal balance between pituitary and adrenal is disturbed, the low output of hydrocortisone causing an increased output of corticotrophin, which in turn stimulates androgen production by the adrenal. Virilisation and a high output of 17-ketosteroids thus occur. It was formerly believed that the salt-losing form of the disorder was due to deficient production of a salt-retaining hormone (since identified as aldosterone). That this is unlikely was suggested by three observations. Firstly, the infants require relatively more deoxycortone acetate to correct the electrolyte disturbance than do adults with Addison's disease. Secondly, the administration of corticotrophin sometimes increases the salt loss. Finally these infants excrete normal, or even increased, amounts of aldosterone.[3] The difference between the "salt-loser" and "non-salt-loser" in adrenal hyperplasia is apparently one of degree. EBERLEIN [7] has shown that, whereas the excretion of pregnanetriol, the metabolite of 17-hydroxyprogesterone, is considerably raised in adrenal hyperplasia (particularly the salt-losing form), that of tetrahydrocortisone, the metabolite of hydrocortisone, is within the normal range when there is no salt loss but is practically absent from the salt-loser. EBERLEIN suggests that in some patients the adrenal, which is tremendously active, synthesises sufficient hydrocortisone to maintain normal electrolyte balance, at the expense of normal growth and maturation; whereas in other patients, where the enzyme defect is more severe, no hydrocortisone can be produced and the electrolyte disturbance occurs in early life. In support of this hypothesis EBERLEIN has found intermediate forms of the disease in which tetrahydrocortisone excretion is low but not entirely absent. These patients are not normally "salt-losers"; but in conditions of stress the adrenals cannot increase their output of hydrocortisone, and electrolyte metabolism is disturbed.

The treatment of acute adrenal insufficiency in infants involves, first of all, rapid administration of large amounts of salt. Hydrocortisone is given intravenously; the soluble hemisuccinate, which can be given in small volume, is a most valuable addition. Deoxycortone acetate intramuscularly should also be given, although it is probably not essential in the less severe cases. Subsequent management will depend on the cause; but in cases due to congenital adrenal hyperplasia, which form the majority, continued cortisone therapy is required both to suppress virilisation and to control electrolytes. Extra salt is needed in the diet in amounts of 2–3 g. daily. Some patients seem to need maintenance therapy, not only with cortisone but also with deoxycortone acetate—which complicates matters because this cannot be administered by tablets to be swallowed. Daily intramuscular injections are unpleasant for both children and parents; but, instead, deoxycortone-tri-methyl-acetate may be injected at intervals of two to four weeks [6] or deoxycortone may be implanted in pellets or adminis-

1. Gordon, M. B. *Advanc. Pediat.* 1942, **1**, 263.
2. Williams, A., Robinson, M. J. *Arch. Dis. Childh.* 1956, **31**, 265.
3. Bongiovanni, A. M. *Pediatrics*, 1958, **21**, 661.
4. Iversen, T. *ibid.* 1955, **16**, 875.
5. Scherz, R. G., Geppert, L. J. *J. Pediat.* 1958, **53**, 645.
6. Wilkins, L. The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. Springfield, Ill. 1957.
7. Erberlein, W. R. *Pediatrics*, 1958, **21**, 667.

tered in a tablet which is held under the baby's tongue until it dissolves.[6] Fludrocortisone, which can be given by mouth and has very potent salt-retaining properties, has not been found an entirely satisfactory substitute for combined treatment with deoxycortone acetate and cortisone; for, when given in dosage adequate to suppress 17-ketosteroid secretion, it has tended to produce hypertension.[8] Small doses combined with cortisone (or prednisolone) may prove more effective.

Annotations

MEDICAL STUDENTS AND SEX EDUCATION

MEDICAL students in general get comparatively little specific instruction on the physiology, pathology, and psychology of sex. Sandler,[9] who sent a questionary to 24 medical schools in Britain and 12 abroad, concluded that "probably less than half of the students at these schools have had anything like adequate instruction before they enter their professional life". No doubt this avoidance of formal teaching is in the English tradition, by which, if anything really matters, the student is left to find it out for himself. But the fact that many young doctors—and some of their seniors—are patently ill-equipped to advise their patients on sexual and marital difficulties has led to a strong demand for more systematic teaching on what is, after all, a not very easy subject. In 1957 a conference of the British Medical Students' Association recommended that such teaching should become part of the curriculum; and last Saturday, at a seminar organised jointly by the B.M.S.A., the Tavistock Clinic, and the Family Planning Association, some senior London students were asked their opinion on how this should be done. The title of the seminar was Sex Problems in Marriage, and the two sessions began with lectures by Prof. W. W. C. Nixon and Dr. H. V. Dicks. After these, groups of about ten students were formed, each with a Family Planning Association doctor and a psychiatrist. The groups had no agenda and their discussions—refreshingly free from English reticence—ranged widely. But there was close agreement on the needs of the medical student. Teachers, it was felt, must assume ignorance of normal sexual physiology and psychology in their students, and should not be afraid of stating the obvious. Also, students should be able to attend demonstrations in contraceptive technique and marriage guidance.

Many of those who spoke seemed to be troubled by the depth of the psychiatric water in which they found themselves. Although it was right in this seminar to emphasise the prevalence of mental dysharmony in marital breakdowns, it would of course be possible to overstress this aspect in undergraduate teaching; for much useful help can be given on a superficial level, especially if the practitioner has confidence in his own knowledge. As to the timing of instruction, many felt it would come too late if given during the clerkship in obstetrics and gynæcology, since patients not uncommonly discuss their marital problems with the student. One solution would be to give an outline of normal sexual physiology and psychology with the clinical introductory course.

If some medical schools are still reluctant to accept these proposals, perhaps it would be useful for the Family Planning Association to run a pilot course in Central London which students could attend voluntarily; but ultimately the responsibility lies on the medical schools themselves. There is much in Professor McLaren's view[10] that instruction is best "integrated into 'medicine'—particularly, of course, into gynæcology and obstetrics"—and not treated as a separate subject.

A REMEDY FOR AGEING?

SINCE Bacon was Lord Chancellor of England, Roumania is probably the only European country which has given high political office, albeit briefly, to a gerontologist. Papers by Parhon on the experimental use of endocrine preparations to modify age changes have been appearing for almost half a century. It is in his school that Aslan and her co-workers have been experimenting with the administration of procaine hydrochloride in geriatrics—work which was reported in 1957 at the Fourth International Gerontological Congress in Merano.[11] The Merano discussions generated more heat than light, and some further information on this work seems to be needed.

Aslan and Vrbiesco[12] originally administered procaine by intra-arterial injection, on the lines of Leriche's studies, to reduce the pain and disability in arthritic conditions. They reported general improvement in the alertness and mood of elderly patients, and in the cachexia which accompanies experimental arthritis in mice.[13] Aslan[14] has now described a six-year study of 20 patients with various non-arthritic senile and presenile disorders who received courses of intramuscular procaine. "Eutrophic" changes, particularly regrowth and repigmentation of hair, and general improvement in wellbeing were noted, and the investigators were sufficiently impressed by these changes to extend their study to 5251 cases of all ages and with many different disorders; 1100 were presenile or middle-aged patients in whom the "prophylaxis of ageing" is being attempted. The treatment consists in repeated courses of procaine: 5 ml. of a 2% solution at pH 4·0 is given thrice weekly by intramuscular or deep subcutaneous injection, with a ten-day interval after every twelve doses. An initial sensitivity test is made with 0·5 ml. Of the many claims of objective improvement the most important concern the physical and mental state of old people.

The cause of the decline of vigour in mammals with age is unknown. There is no a-priori reason why procaine, or many other uninvestigated substances, should not slow or even reverse this decline, and a substance which did so would quite possibly produce just the kind of non-specific benefit in a number of disorders which Aslan describes. The regrowth of pigmented hair in a man who claimed to be 110 years old, which Aslan reports, would in any case, like the validity of the age-record, excite curiosity. But it is curiosity rather than enthusiasm that Aslan's treatment of her results is likely to excite. Her suggestion that procaine acts by in-vivo conversion to *p*-aminobenzoic acid, and that this exercises a "trophic" action on the nervous system, does not carry instant conviction; moreover, such an influence (or, in fact, any specific benefit

8. Grumbach, M. M., Wilkins, L. *ibid.* 1956, **17**, 418.
9. Sandler, B. *Lancet*, 1957, i, 832.
10. McLaren, H. C. *ibid.* 1957, i, 935.
11. Aslan, A. *Int. Congr. Geront.* 1957, p. 468.
12. Aslan, A., Vrbiesco, A. *Bull. Sci. Acad. R.P.R.* 1950, **2**, 891.
13. Aslan, A., Nedler, M., Todea, I. L. *Commun. Acad. R.P.R.* 1951, **1**, 1111.
14. Aslan, A. *Therapiewoche*, October, 1956, p. 14.

from a drug administered to geriatric patients to control "ageing") could be shown convincingly in one way only—by a double-blind trial in alternate matched cases, with subsequent comparison of objective signs and survival curves. All the published evidence so far depends on scientific medicine's chief methodological enemy—the testimonial use of case-histories—and Aslan's treatment of these will depress those who know how often medical investigators have misled themselves in this way. There are very few old people who do not respond to rest, change, good hospital food, and, above all, raised morale—whether accompanied by injections of procaine or not.

This is not to say that the work of the Bucharest team is to be dismissed (they have evidently improved their patients in some way, if only by suggestion); and the desire to do something radical about old age is a creditable contrast to fatalism about the effects of age. If these workers were right, the findings would be important. But the facts can be established only by properly controlled trials.

FLUORIDATION IN NEW ZEALAND

THE controversy over the fluoridation of water-supplies continues, and public opinion has already caused the abandonment of more than one project in this country. We have heard of some of the difficulties of introducing fluoridation in the United States,[1] and in particular of the determined stand by New York State. Eighteen months ago, a commission appointed by the New Zealand Government [2] recommended that fluoridation schemes should be started as soon as possible, and that these schemes should be carried out by the local authorities. This year, however, a petition is to be presented to Parliament asking the New Zealand Government to make fluoridation illegal. Compulsory mass "medication" has never been popular (one instance is the outcry against iodised table salt), and a discussion of its ethics usually leads to an interminable wrangle in which the real issue tends to be obscured by emotion. The strength of the case for or against fluoridation depends on the answers to two questions: can it do harm, and does it do good?

Fluorine and its compounds are, of course, highly toxic; and many of the objections to fluoridation are based on the possible ill effects of the long-continued ingestion of fluorides, even at the recommended level of 1·0–1·5 parts per million (p.p.m.). There seems to be an unfortunate association in the lay mind between fluorides and the destruction of cockroaches. Those better informed believe that danger may lie in the deposition of fluorides in the skeletal system, leading to arthritic changes, particularly in the lumbar spine, and to further damage to already diseased kidneys. In reality, such ill effects from fluoridated water have not been observed. Those who live in the high-fluorine areas of this country (4 p.p.m. and over in the water-supply) are apparently as healthy as anybody else, although their dentitions will undoubtedly show signs of fluorosis.[3]

On the engineering side, one difficulty is in metering fluorides accurately into the water-supply—even the well-established chlorination plants can be temperamental, and fluorides present their own special problems.[4] In Hastings, New Zealand, the first equipment to be installed fed solid sodium silicofluoride into the water, but it proved to be incapable of maintaining optimum concentration. (The plant usually delivered less than the desired amount of fluoride.) The equipment was used only intermittently until the end of 1954, when it was replaced by one using liquid sodium fluoride. Since then the fluorine content of the water has remained within the limits suggested by the New Zealand Department of Health—1 p.p.m. ±10%. Assuming that fluoridation at this level (or even at one of 1·5 p.p.m.) is safe, treatment of the water-supply would seem to be more satisfactory than giving the public tablets of sodium fluoride, with the attendant risks of over or under dosage.[5] But the tablet method has some advantages: only those who wish to consume fluoridated water need do so; since the effects of fluorides on the teeth appear to be negligible after 16 years of age, only the age-groups affected need receive fluoride; and possibly the cost to public funds might be less than that of fluoridating the water.

Not all the reports on the action of fluorides in raising caries-resistance agree on the extent of protection, but it seems almost indisputable that fluoridation is beneficial. A report from Hastings, New Zealand [6] which, like Australia, is notorious for having an extremely high incidence of dental caries, probably because of the low fluorine content of all water-supplies,[7 8] corroborates the findings in other countries.

The Hastings project dates from 1951 when—in the absence of much information about the effects of fluorine—it was decided to confirm published results by means of a local study. Hastings is a town with a population of about 20,000, and the water-supply comes from an artesian source with a natural fluoride content of 0·15 p.p.m. The first fluoridation plant, installed in 1953, did not prove satisfactory. The new plant was installed in September, 1954, and since then the fluorine content of the water has been kept at about 1 p.p.m. in all parts of the town.

The original intention was to assess the effectiveness of fluoridation by comparing the caries experience in Hastings with that in the adjacent town of Napier—a method used in the United States in the Newburgh-Kingston study.[9] But the incidence of caries in the two towns was found to be quite different, and some time elapsed before it was discovered that this discrepancy arose from differences in the basic soil types in the two areas. Unfortunately, the report does not make clear where this difference lay—whether it was a matter of fluorine content or whether other mineral substances were present in the Napier water but absent from that at Hastings. The effect of fluoridation was assessed by comparing the caries-experience of Hastings children before fluoridation with that of a comparable group of children after fluoridation.

The "control" group were examined at the end of 1954; these children, aged 5–16, were of white parentage, had lived in Hastings all their lives, and had consumed only the public water-supply. They had received intermittent supplies of fluorine from the original plant for about eighteen months. The other group, which obviously included some of those seen in 1954, were inspected at the begining of 1957, when they had all been receiving fluoridated water for twenty-seven to thirty months longer than the "control" group.

The reduction in the amount of caries in the children aged under 9 years in 1957 was striking, amounting to about 42% in the permanent teeth of children aged 6, about 39% in those aged 7, and about 18% in the 8-year-olds. In children over 9, a slight reduction in the amount

1. Mackenzie, E. F. W. *Lancet*, 1952, i, 961.
2. See *ibid.* 1957, ii, 933.
3. *ibid.* 1956, i, 745.
4. The Fluoridation of Domestic Water Supplies in North America; p. 64. H.M. Stationery Office, 1953.
5. See *Observer*, Sept. 2, 1956; *ibid.* Sept. 30, 1956.
6. Ludwig, T. G. The Hastings Fluoridation Project. New Zealand Department of Health, Wellington, 1958.
7. Chamberlain, G. *N.Z. J. Sci. Tech.* 1946, **B28**, 154.
8. Denmead, G. *ibid.* p. 158.
9. Ast, D. B., Finn, S. B., McCaffrey, I. *Amer. J. publ. Hlth*, 1950, **40**, 716.

of caries was noticed, but not enough to be statistically significant. The deciduous teeth showed improved resistance to decay in those aged 5, in whom the reduction amounted to about 14%. Analysis of the results for individual types of tooth confirmed the results for the dentition as a whole, and the reduction in caries experience was shown to be due primarily to the increased resistance to attack of the first permanent molars.

The first permanent molar has been called, rather fancifully, the "keystone of the dental arch": possibly the bad effects of its early loss have been exaggerated, but nevertheless it is a valuable tooth. Fluoridation also affords some protection to the second permanent molars and to the permanent incisors.

DIAGNOSIS OF PLEURAL EFFUSION

FURTHER evidence of the value of pleural biopsy [1] in the early diagnosis of cases with pleural effusion is coming in. Discussing biopsy techniques (prescalene node, pleura, and lung) in intrathoracic disease, Breckler et al.[2] suggest that pleural biopsy will give the diagnosis in 80% of cases where the effusion is caused by tuberculosis, if the biopsy is timed correctly; but they have evidence that chemotherapy will bring about complete resolution, so that diagnosis may be impossible if the biopsy is delayed, while at an early stage lymphocytic infiltration alone may be found. Donohoe et al.[3] point to the difficulties and delays with the older methods of diagnosis. They find that aspiration biopsy can give a definite diagnosis even before the first twenty-four-hour sputum specimen has reached the laboratory: in a series of 45 patients, a definite diagnosis was obtained in 83% of those with suspected tuberculosis and in over 50% of those with suspected neoplasms; in a group of "indeterminate" cases (not consistent with a clinical diagnosis of either tuberculosis or malignancy), biopsy provided the diagnosis in 54%. Of 13 patients in all groups in whom biopsy showed non-specific changes, 10 were subjected to open surgical biopsy; in 7 this yielded the diagnosis, but in the remaining 3 even complete exploratory thoracotomy gave no definite information. These workers now resort to open surgical biopsy only after at least three aspiration specimens have failed to lead to a specific diagnosis. Equally convincing are the reports of the preliminary [4] and detailed [5] results in a period of less than two years on 200 patients (mostly from the Services) in this country: Mestitz et al.[5] used the Harefield needle,[6] which enables aspiration of the pleural fluid and a punch-biopsy of the pleura to be carried out in one operation; they show that this method can give the diagnosis early in 80% of tuberculous and 60% of malignant cases, and suggest that it should be part of the initial investigation of every patient with a pleural effusion of uncertain origin. If the first specimen is negative, a second should be obtained; but of 228 specimens only 8 were inadequate. This method will not entirely eliminate the need for surgical biopsy, but the number of these can be much reduced.

Not satisfied with the 80% success-rate in the diagnosis of tuberculous pleural effusions by needle biopsy, Schless et al.[7] have reviewed the records of 63 patients who underwent open thoracotomy on account of pleural disease at an Army hospital. In only 17 of these patients was the thoracotomy carried out primarily for diagnostic purposes; in the remainder it was partly or mainly therapeutic (e.g., for decortication). Of the 38 patients ultimately diagnosed as having tuberculosis, many had been on chemotherapy for periods averaging six to nine months. Thus, the claim by Schless et al. that thoracotomy and surgical biopsy will give the diagnosis in 92% of cases of tuberculous effusion refers to a quite different type of material from that in the aspiration-biopsy series. Of the 25 non-tuberculous cases, 7 showed no accompanying pulmonary lesion and were diagnosed as non-specific pleural effusion (Mestitz et al.[5] found 2 such in their series), while 7 had a history of pneumonia, 3 had surgically proved bronchiectasis, 1 had rheumatoid arthritis, and others had fungus infections. The impression from this work is, not that thoracotomy should compete with aspiration biopsy in the early stages of a pleural effusion, but that when the early biopsies (perhaps two or three) and other investigations are negative thoracotomy with open surgical biopsy of the pleura and of any diseased part of accessible lung will help considerably in diagnosis.

1. See *Lancet*, 1957, i, 147.
2. Breckler, I. A., Hensler, N. M., Hill, H. E., Hoffman, M. C., Hukill, P. B. *Ann. intern. Med.* 1957, **46**, 706.
3. Donohoe, R. F., Katz, S., Matthews, M. J. *Amer. J. Med.* 1957, **22**, 883.
4. Mestitz, P., Pollard, A. C., Purves, M. J. *Lancet*, 1957, ii, 873.
5. Mestitz, P., Purves, M. J., Pollard, A. C. *ibid.* 1958, ii, 1349.
6. Abrams, L. D. *ibid.* 1958, i, 30.
7. Schless, J. M., Harrison, H. N., Wier, J. A. *Ann. intern. Med.* 1959, **50**, 11.

THE CHILD WHO DISAPPOINTS

THE Pædiatric Section of the Royal Society of Medicine enjoyed a lively evening when, on Feb. 27, it discussed the Child Who Could Do Better at School.

Dr. A. Doyne Bell described the problem as troublesome and unlimited. Although he believed that physical factors were less important than social and psychological ones, partial deafness was a ready cause, and he was glad that audiograms were done so commonly nowadays: visual defects could also go unnoticed. He had seen cases of chronic illness—e.g., of cœliac disease—brought eventually to light through scholastic failure. Bright children could fail because of environmental faults, and the parents were clearly vitally important; a school report of thirty years ago said: "This boy gives little trouble and takes less: he will make an excellent parent." The uninterested parent who misapplied parental control might encourage a child to truancy by making him help with the baby-minding or shopping; and there were the problems, too, of sleep lost while hanging around outside public-houses and of squalid overcrowded dwellings. At the other extreme was the ambitious parent whose child, however brilliant, could always "do better". Dr. Doyne Bell wondered how great was the adverse effect of large classes and poor school buildings, and whether in the vast new schools fewer children would fall below expectations—an important point which was unfortunately not taken up. Doctors had some responsibility: for instance, he had known rarely of a doctor's certificate being a cover for truancy, and the ability of an epileptic might be impaired by over-prescribing anticonvulsants.

Mr. Edward Blishen, speaking of his experience of teaching the duller secondary-school boys in a poor district, said that the majority could do better; and the main reason was a social one. Whereas in the elementary school a child might do well, the transition at 11 to a place among bigger boys where the teachers were more formal and less "parental", together perhaps with excessive growth (which might take the "edge" off a boy), often caused a promising pupil to "grind to a halt". Before, living was learning and learning was living; but the new curriculum did not strike a chord. The lad saw his parents coping with life possessed of a short sharp range of useful

knowledge, but illiterate beyond everyday needs: such a home did not stimulate the boy to take in information, and he readily came to scorn the teacher's " effeminate anxiety for knowing the unnecessary ". The motivation for learning was then moribund if not actually dead, and the school did not manage to awaken the child's awareness of need to learn. There must be identification between school and environment; and social workers should bear this in mind, for the conflicting demands of home and school could impose appalling strains.

In schools such as his, divided into 4 streams, it was usually thought hard to teach streams C and D; but he had found most resentment of schooling in A and B, and B was the hardest of all to teach, being a no-man's land between the able and the dim. Personally he preferred teaching C and D; for, if a positive approach was made, they responded in a pathetically enthusiastic way. Left at the elementary-school stage, they longed to master the simple skills and still had about them the small child's curiosity that was usually satisfied in the junior school. Their need for praise was great, and the right approach involved time and affection. It was hard to take a large class, and teachers were overworked. This was sad, for it was amazing the progress a boy might make if the teacher could spare time to sit beside him so that they could go through the work together. This was especially important for the child unable to master some skill—maybe a very small one—for discouragement tended to spread and he might mark time at that point. Training-colleges, added Mr. Blishen, prepared the young teacher inadequately in such important topics as delinquency and backwardness.

Mr. H. A. T. Child, headmaster of Dartington Hall School, mentioned the child that could do worse. The rat-race ideology in schools led to children being pushed harder than they should be. Studies of intelligence quotient and attainment had shown as many children doing *better* than was expected as were doing worse. The I.Q. was a fallible index and might not have much to do with a child's potentialities. Research before the late war had suggested that some two-thirds of all backwardness was due to dullness, whereas post-war the proportion was down to about half. Some causes of backwardness were increasing, and Mr. Child suggested that the emotional disturbances of the war played a part—an observation which fits in with the increase of delinquency in this age-group. Such incomplete development might be found at any level: for instance, in the grammar school where the brilliant child might appear only average.

Supporting Mr. Blishen's view of causation, Mr. Child cited a study of backwardness in the 800 primary schools in London. Backwardness was maximal at the centre with four prolongations to the north and two to the south, all several miles wide and corresponding to the main railway lines. The disproportion between areas was such that a child born in some places had as little as 1 chance in 400 of gaining a grammar-school place. Mr. Child believed, too, that the culture in such places was antipathetic to education.

Turning to private schools, he said that he suffered constant pressure to accept children who had failed elsewhere. He had observed two periods of crisis—the first at 9–10 when the child was being crammed for the common-entrance examination, and the second at 14 when G.C.E. came into view. The teachers became anxious and transmitted their anxiety to child and parents. This problem was more severe than was realised; even children with I.Q.s of 130–160 could break down under the academic strain. The ambitious father was the biggest factor. Most often he was either a very successful man who expected his son to succeed too, or else an unsuccessful one who wanted the boy to make up for his failures. Schools taking boarders were often offered children whose parents were separating; and such a child might seem to have no drive or interest, absorbed as he was with the collapse of his world. The parents, feeling guilty, made matters worse by over-indulgence.

Presenting the psychiatric view, Dr. R. F. Barbour recommended simple screening measures, such as reading-cards and sentence-completion tests. The hyperkinetic child with an abnormal electroencephalogram should be watched for, as he might benefit greatly from amphetamine. Phobias of school arose from maternal over-protection and could be centred on things such as changing for gym or the swimming-pool; tranquillisers helped some of these children. Dr. Barbour regarded the passive obedient child with especial gloom: subjected to excessive pressure by his parents, he retired behind his books to a quiet ineffectual fantasy life where he could " control the world ". Hospital attendance was sometimes a factor in failure; even half a day a week for such things as remedial exercises might ruin a term's work. Only a small proportion of children and parents needed intensive treatment, and child-guidance facilities were usually good; family guidance was increasing, but in all cases there was need for close liaison with the general practitioner, who knew the family situation and might spot the difficult child in preschool years.

Sex, coeducation, and delinquency were scarcely touched on—oddly perhaps, for the well-known discrepancy between verbal and performance I.Q. in delinquents suggests that these, as a group, could do better academically. Nor is this surprising; for " To learn by example is to submit to authority." [1] It will, however, have been a pleasant surprise to physicians leading cloistered lives to find teachers so acutely aware of emotional and social factors. Perhaps this meeting will foster collaboration between pædiatricians, psychiatrists, psychologists, educationists, and sociologists. In this field too much work has been isolated and sectarian, and yet nowhere is a multidisciplinary approach more essential. In Britain we have a unique opportunity for study and comparison of educational methods, for this country has every kind of school from the free-for-all coeducational experiment to the old authoritarian segregated public school. New ideas on education surround us in bewildering profusion, virtually undocumented save for a few enthusiastic volumes. Does school experience influence personality or sexual orientation, for example? No-one really knows. It might be said that our entire educational system is " experimental "; and the sooner we start assessing the results, the better.

1. Polanyi, M. Personal Knowledge. London, 1958.

THE INDEX and title-page to Vol. II, 1958, which was completed with THE LANCET of Dec. 27, is to be issued next week. A copy will be sent gratis to subscribers on receipt of a post-card addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Special Articles

THE PSYCHOPATH AND THE MENTAL HEALTH BILL

MAXWELL JONES
C.B.E., M.D. Edin., M.R.C.P.E., D.P.M.
DIRECTOR

FERGUS STALLARD
M.B. N.U.I., D.P.M.
SENIOR HOSPITAL MEDICAL OFFICER

ISOBEL H. HUNTER
M.A., M.B. Glasg., D.P.M.
SENIOR REGISTRAR

RONALD A. BROOKES
M.B. Sydney
REGISTRAR

From the Social Rehabilitation Unit, Belmont Hospital, Sutton, Surrey

THE new Mental Health Bill describes psychopathic disorder as

" persistent disorder of personality (whether or not accompanied by subnormality of intelligence) which results in abnormally aggressive or seriously irresponsible conduct on the part of the patient, and requires or is susceptible to medical treatment ".

This description will satisfy no-one, but it is at least an attempt at a working definition. It does seem to imply that admission for treatment need not be limited to the dangerous criminal psychopath who is physically assaultive; for it apparently covers also the more familiar inadequate types who are characteristically found at psychiatric outpatient clinics.

How Many ?

The number of psychopaths is not known. Many are seen in courts, and others at psychiatric clinics; but an unknown number drift along without ever coming before any medical or legal body. An unknown number are in our prisons. Some are to be found in mental hospitals (one big hospital of 2000 beds has 40 patients diagnosed under this heading) and some are in mental-deficiency colonies. If the Bill becomes law in its present form, probably patients of reasonably high intelligence who have been certified under the headings like " moral deficiency " or " mental deficiency " will be discharged when they reach the age of 25. Moreover, as public knowledge of mental health problems grows, and people are beginning to see that antisocial behaviour may be due to psychological causes, more patients with this disorder are probably seeking help at psychiatric clinics, magistrates courts, or welfare agencies. At Belmont Hospital about the same number of these patients reach us from the courts as from psychiatric clinics.

Problems of Compulsion

Under the Bill admission to hospital for either observation or treatment will call for two medical certificates, one of them from a psychiatrist. Admission for observation will be for a period not exceeding twenty-eight days and can be arranged for a patient of any age. For treatment, on the other hand, only psychopaths under the age of 21 will be admitted, and the Bill lays down that psychopathic patients already in hospital shall be discharged on reaching the age of 25 unless it can be shown that they are likely to be a danger to other people or to themselves. A patient who is detained on these grounds has a right to appeal to a mental-health tribunal. Since obviously a patient does not cease to be psychopathic at the age of 25, this provision may create some headaches for doctors in hospitals and for the tribunals.

Diagnosis is often very difficult; and in a doubtful case a period of observation may well be necessary if the medical certificate for compulsory treatment is to be signed in a responsible way. Indeed the whole question of compulsion and psychopaths is full of complexity. As the Royal Commission [1] pointed out, " If psychopathic patients are subjected to special forms of compulsion on grounds of abnormality which is evidenced mainly by their behaviour this is almost equivalent to the creation of a special quasicriminal code for them alone." The fact that the decision to detain an unwilling patient will now be a purely medical decision will create serious problems for the doctor, at any rate until the practice becomes familiar and established. One of the doctors who signs the certificate has to be a psychiatrist, and he may be the doctor at the mental hospital where the patient will be treated. Clearly this type of patient will already be resentful of authority, and the doctor who has deprived him of his liberty may be at a grave disadvantage in treating him.

Compulsion will in practice probably be most useful for patients referred from the courts and prisons. Most non-criminal psychopaths who need help might well be prepared to accept treatment willingly if there were adequate facilities for treatment; but unfortunately these are as yet almost non-existent.

Proposals for Psychopathic Units

The Bill makes the procedure for admission to psychiatric hospitals or units more flexible, and these establishments are no longer obliged to accept patients. It is reasonable to suppose that psychopaths will be the patients most likely to be refused admission because of their known nuisance value and the disturbance which they cause not only to other patients but to the staff.

In the opinion of many psychiatrists, to admit these patients to ordinary mental-hospital wards is to create an undesirable situation. They usually derive little benefit and their tendency to act out their difficulties by antisocial behaviour tends to be seen as mere " badness ", to be dealt with by disciplinary measures and appeals for good behaviour. If the ward is organised on group treatment lines, then the psychopath, even in a ward containing mixed diagnostic categories, may be helped to examine his behaviour and its effects on other people. At the present stage of our knowledge, however, we should prefer to see a few pilot units established to study the treatment of psychopaths as a special group. Such units would probably need to be both closed and open, because many patients diagnosed as psychopaths will be directed to hospital voluntarily, and relatively few will be of the dangerous criminal type which the public, and perhaps many psychiatrists, understand by the term psychopath. Our own experience is that many of these patients can with advantage be housed in an open unit, though we always have many patients who would be possible subjects for compulsory treatment under the Bill.

Siting

An important question is the siting of these units. If they were attached to psychiatric hospitals, there would

1. Royal Commission on the Law Relating to Mental Illness and Mental Deficiency. H.M. Stationery Office, 1957.

be obvious gains in economy and in sharing specialist medical services. More important is their attachment to an ongoing psychiatric service with its established traditions, its own catchment area, and its contacts with the local authorities, general practitioners, and others. Moreover, the psychiatric hospital would be already familiar in the neighbourhood, and the addition of a psychopathic unit would be less challenging than a new establishment solely for the treatment of psychopaths. For satisfactory treatment, however, such units must be relatively small and as self-contained as possible. They will need a specially trained and relatively numerous staff, probably with a much higher staff-patient ratio than in the parent hospital. This means the creation of a difficult minority problem. The psychopathic unit would tend to be seen as privileged, "different", dangerous. Moreover, the psychopath, in our opinion, should be treated in a democratic equalitarian community [2-4] and this would often conflict with the treatment pattern of the parent hospital. Two separate treatment ideologies within the same hospital must certainly lead to difficulties. On the other hand, there are already in this country several mental hospitals (notably Netherne and Claybury) with "therapeutic communities" which have "budded off" and, despite some resistance, have achieved their own distinctive therapeutic culture.

The alternative is to have separate psychopathic hospitals which would develop their therapeutic culture unhampered by the established treatment ideology and mores of a parent hospital. To start a new venture with the opportunity to acquire appropriate staff would offer a great opportunity for initiative. The psychopath needs no physical therapies and the trained nurse might be no more appropriate for their treatment needs than, say, someone trained in the social sciences. In view of the shortage of nurses it might be both expedient and suitable to recruit trainee probation officers, prison officers, psychologists, social workers. Training in group work would need uninterrupted service for at least six to nine months. With relatively articulate and active patients there would be a great incentive to develop community activities, and the community might go a long way towards being self-supporting. One danger would be isolation from the general body of psychiatry, as happened to some extent with mental-deficiency hospitals. Moreover society might be tempted to deal with an unpleasant and frightening problem by isolating it as, until recently, it isolated mental patients. Probably, therefore, independent psychopathic units should be centrally situated, with good communications with the town or towns which they serve so that the families can remain in touch with the patients.

Our own experience would favour units of not more than 100 patients; preferably of both sexes, if the patients were over the age of 18. It is possible to have some awareness of the outstanding personality characteristics of 80–100 people. Moreover a unit of this size is big enough to have diversified subgroups and a considerable overall "public opinion". The staff needed would be big enough to include people with various trainings and to allow for the development of a highly integrated team. Mixing of the sexes seems to give a more normal community, with better opportunities for social rehabilitation than an all-male or all-female population.

Treatment

In our unit at Belmont Hospital we have developed community and group methods of treatment because they seem appropriate to this type of patient. At present it is only possible to aim at humble treatment goals—e.g., changes in social attitudes rather than fundamental personality changes.

It is difficult to describe a therapeutic community briefly, but it is distinctive in the way the institution's total resources, both staff and patients, are consciously pooled to further treatment. This implies a change in the usual status of patients. In collaboration with the staff they become active participants in the therapy of other patients and in other aspects of hospital work—in contrast to their more passive recipient role in conventional treatment regimes. The basic problem in psychopathy centres round difficulties in social relationships. The patients feel isolated and suspicious, fearful of a society which they see as punitive and rejecting. Somehow they have to be helped to look at their behaviour and become aware, at least in part, of their motives. They must be helped to feel secure enough to express their feelings in groups and to feel identified with the unit. This often leads to an awareness of their social attitudes and a comparison with those held by most of the staff and patients. In this way they can be helped to modify their attitudes. The social organisation of the unit affords opportunities for playing many and varied roles, and patients may come to experience social responsibility in a way new to them.[5]

The full participation of the patient population is essential. Patients must be faced by the effects of their behaviour on other people and helped to see what they have done. They are more attentive and receptive to their peers than to authority, and we have found that daily meetings of all patients and staff help to bring the patients into active treatment, not only in relation to themselves but in relation to their peers.[2-4]

Staff Training

In psychopathic units selection and training of staff are very important. The patients make heavy demands on staff for patience and understanding. People exposed to this type of behaviour for long periods—especially the nurses—cannot be expected to retain their emotional balance and interest unless given continuous support and adequate training. We have found it necessary to hold daily seminars at which the nurses can discuss their relationships with the patients. This serves as a useful feedback of information about the patients. If the seminars are skilfully handled, the nurses come to feel secure enough to describe something of their own subjective feelings both in relation to the patients and to their colleagues. In this way they come to learn something about transference and counter-transference and about group dynamics. We believe that similar training facilities are necessary for all those in contact with the patients—e.g., workshop instructors. Training of this kind takes time, and at least six to nine months is necessary to understand basic principles. The usual three-month stay of a student nurse would be impracticable in this type of unit and harmful to the patients' treatment.

2. Jones, M. *Amer. J. Psychiat.* 1956, **122**, 647.
3. Jones, M. *Psychiatry*, 1957, **20**, 211.
4. Jones, M. Social Psychiatry. London, 1953.
5. Parker, S. *Brit. J. Deling.* 1957, **7**, 285.

Diagnostic Centres

The Royal Commission's report stressed the need for centres to which patients could be referred from courts or hospitals for medical, psychological and social assessment. The Mental Health Bill makes no mention of such centres, for they do not come within its terms of reference. But it would be a pity if the idea were dropped, for there is a great need for several centres of this kind. Properly staffed, they would allow the provision of compulsory admission for observation for a period of up to twenty-eight days to function effectively, and many unwilling patients might become reconciled to treatment voluntarily after an observation period in one of them. They would also be a safeguard for the correct use of long-term compulsory treatment, and would promote liaison between the health service and the prison service. The Bill itself offers scope for court referrals for hospital treatment and for the transfer of prisoners to an appropriate hospital outside prison. Referral of willing patients from psychiatric outpatient clinics for classification and guidance about appropriate treatment would also be possible.

These centres could become invaluable for standardising classification and for research. They would also be valuable for training staff, but it is doubtful if they could usefully serve as diagnostic and treatment centres at the same time.

Research

Little basic research on psychopathy has as yet been done in this country. The most urgent questions centre round the size and nature of the problem and response to treatment. The framework provided by the Bill makes possible various patterns of treatment, which might be tried by different regional boards. This should make possible much-needed control studies. In the first instance it might be better to start with one or two pilot treatment and diagnostic centres administered by the Ministry of Health, backed perhaps by one or several of the large research organisations.

Without careful planning and skilful use of our limited number of experienced staff, harm rather than good might come from hasty application of the provisions of the Bill. Moreover the Royal Commission's report, where it touches on the problems of the psychopath, is probably ahead both of general and of psychiatric opinion, and, unless due circumspection is used, reactionary forces may block fulfilment of many objects of the Bill.

If psychopathic units are not to be adequately staffed, it would be better not to attempt the treatment of psychopaths at all. Merely to refer them to ordinary mental hospitals, in the hope that they would get proper treatment, would be disastrous. It might lead to some psychopaths being segregated indefinitely in hospital.

Aftercare

We have come to feel that proper provision for selective aftercare is vital to the treatment of psychopaths. The critical period seems to be the three months after leaving hospital. But many patients will remain only marginally adjusted all their lives. Others will be frank failures but will still need the help of social agencies if their families are to be saved from complete disintegration. This will probably prove to be the most rewarding if at the same time the most disheartening part of work with psychopaths.

Medical Education

EFFECTIVE USE OF TEACHING TIME

C. R. B. JOYCE
M.A. Cantab., Ph.D. Lond.
LECTURER

M. WEATHERALL
M.A., D.M., B.Sc. Oxon.
PROFESSOR

DEPARTMENT OF PHARMACOLOGY,
LONDON HOSPITAL MEDICAL COLLEGE, LONDON, E.1

MUCH of the preclinical medical course can be taught in more than one way—by lectures, seminars, and practical classes, or by leaving students (under some guidance) to read the subject for themselves. We have previously attempted to compare the relative usefulness (estimated by the ability of students to pass examinations) of some of these methods (Joyce and Weatherall 1957). We pointed out that the economy of the methods (the total time taken by students and teachers together in achieving the same results) differed, and that it was important (and certainly more realistic) to assess the usefulness of combinations of methods in teaching. Many different combinations could be tried; adequate testing of them all would take longer, or require the participation of more students than are available in one department of one medical school. It seemed most useful to compare methods in which the contribution of teachers' time (often a limiting factor) was small, with others in which teachers were involved more fully. From the students' point of view such methods can perhaps be classified as "do-it-yourself" or "have-it-done-for-you". Passive acceptance of explanations may give less mastery of material than does active manipulation by the students (Cronbach 1954, Laner 1955). On the other hand, the presence of a teacher may restrict the active participation of some students, perhaps especially those who most need encouraging. Whether participation as such leads to success is a matter of dispute (Asch 1951, Wispé 1951 and 1953, Smith 1955); and in any case medical students have not been studied in this way. We have therefore examined the usefulness and relative economy of teaching groups of students by passive or active means, using the objective methods already described (Joyce and Weatherall 1957) for assessing the results.

Methods

62 students in the third term of their 1st preclinical year attended a course on the pharmacology of the peripheral nervous system. Basic information was given in four 1-hour lectures. Before the course began, the students were allotted to 4 groups with a similar proportion of students of different abilities (judged by their previous performance in class examinations in physiology). 2 such groups took part in three practical classes, while the other 2 groups watched corresponding demonstrations. 1 group taking practical classes, and 1 group watching demonstrations attended seminars of the conventional kind; the other 2 groups each held three free discussions which were initiated by playing back short talks recorded by a tutor.

For these 2 groups there were four talks, of which the first contained instructions and suggestions for procedure; the second was a mainly factual and very condensed account of the pharmacology of the autonomic nervous system; the third described clinical applications of this knowledge; and the fourth was intended to stimulate discussion of some wider biological aspects of the subject. Each discussion group was shown how to operate the apparatus and left to use the material as its

members wished. A teacher was available in a nearby room, and the students were told they might consult him if they desired. In practice they seldom sought his advice during the sessions. Attendance was not compulsory, and no formal records were kept, but the teachers' rough estimates suggested that there were rarely, if ever, more than 2 students absent from any group. In order to minimise the differences between teachers, their contributions were balanced as evenly as possible (table I), save that one gave all the lectures and another was assisted in practical classes by two additional demonstrators. Each tutor recorded two of the four talks.

Before and after the course all groups were tested by an objective examination. Beforehand each half of the class was given half of the examination. The halves had been matched for item-difficulty on the basis of previous experience with the same material. At the end of the course, the whole class was examined on all the material.

Test A was a prose test, and tests B and C each contained sixteen 4-part multiple-choice questions; those of test C were designed to show the candidate's ability to handle logical relationships as well as purely factual material (Joyce and Weatherall 1957). Test D contained sixteen 6-part multiple-choice questions. A, B, C, and D tested knowledge of the peripheral nervous system; test E contained sixteen 4-part multiple-choice questions about statistics and quantitative biological methods, based on a course given by the same teachers to the same students in their first term, but upon

TABLE I—EXPERIMENTAL DESIGN

Day	Group I	Group II	Group III	Group IV
1	←	Test[AB]		→
	←	4 lectures[A]		→
2-9	3 demonstrations[A]	3 practicals[B]	3 demonstrations[A]	3 practicals[B]
	3 discussions[A]	3 discussions[B]	3 seminars[B]	3 seminars[A]
10	←	test[B]		→

A = supervised by tutor A.
B = supervised by tutor B.

which they had not been previously examined, and upon which no further teaching was given during the experimental course described here. This was intended to measure roughly the effect of practice on the test results. 10 minutes were allowed for answering section A, and 70 minutes for the full sections B, C, D, and E together.

Before the course began, all students were given a blank time-sheet on which they were asked to record in detail how they spent their working hours—reading text-books, writing up notes, and so on. At the end of the course, these sheets were collected, together with students' criticisms and comments. The design of the experiment is shown in table I.

The value of the course was assessed by the gain in knowledge, by the time required to achieve similar ends in different ways, and by the views and attitudes of the students.

TABLE III—MEAN IMPROVEMENT OF ALL STUDENTS TAUGHT BY EACH METHOD (%)

Groups	II+IV	II+III	III+IV	I+II	Mean
No. of students	25	28	30	23	53
Test	Practicals	Demonstrations	Seminars	Discussions	—
A Prose	34	40	37	42	39
B 4-part	30	32	28	35	31
C 4-part: "logical"	42	43	42	44	43
D 6-part	23	23	22	24	23
E 4-part: "control"	7	1	7	0	4
Mean of B, C, and D	32	33	31	34	32

Results

Usefulness of Teaching

In table II are summarised the mean marks obtained by the students in each of the 4 groups tested at the start and at the end of the course.

The marks have not been corrected for the probability of guessing the correct answer by chance in the multiple-choice sections; this affects all candidates equally, and the expected chance score for a single candidate is 25% in sections B, C, or E, and 17% in section D. In section A there is no chance score, though an uninformed person could probably score 5 or 10% by intelligent guesswork.

The individual scores are so widely scattered (both at the initial and final tests) that only the differences between individuals and between the sections of the test are significant at conventional levels ($P < 0.01$).

At the initial test, the marks obtained on sections B, C, and D are little above chance, and they presumably reflect a level of initial ignorance that is at least satisfactory for the experiment; the marks for section E are appreciably higher, as would be expected for material that had been previously taught. Group I (demonstrations and discussions) made the greatest improvement of the 4 on sections B, C, and D, followed by group IV (practicals and seminars). There was little difference between groups II and III. There was little overall improvement on section E (and indeed a small loss by group I) which suggests that the effects of practice upon the tests used were very small.

Table III shows the mean improvement mark by all students taught by each of the four methods. Although those taught by demonstrations and discussions scored higher than those taught by practicals and seminars respectively, the differences are not significant. It can be concluded, however, that teaching by means of tape recorders or by demonstrations is at least not inferior, and may even have a small advantage over the other methods.

It could be argued that the similar degree of improvement shown by all groups is due to the fact that almost all the information tested was obtained from lectures, rather

TABLE II—MEAN TEST SCORES AND MEAN IMPROVEMENT BETWEEN TESTS (%)

Group	I			II			III			IV			Mean		
No. of students at both tests	12*			11*			16			14			53		
Method	Demonstration/ Discussion			Practical/Discussion			Demonstration/ Seminar			Practical/Seminar			—		
Test	Before	After	Improvement	Before	After	Improvement	Before	After	Improvement	Before	After	Improvement	Before	After	Improvement
A Prose	51	91	40	44	88	44	48	88	40	50	85	35	49	88	39
B 4-part	21	65	44	27	52	25	36	59	23	24	58	34	28	59	31
C 4-part: "logical"	29	80	51	32	69	37	34	72	38	28	74	46	31	74	43
D 6 part	20	51	31	21	36	15	22	39	17	15	44	29	19	43	24
E 4-part: "control"	59	56	−3	53	57	4	49	53	4	50	61	11	53	57	4
Mean of B, C, and D	23	65	42	27	52	25	31	57	26	22	59	37	26	58	32

* Smaller numbers due to non-attendance at the first test.

TABLE IV—HOURS SPENT IN ATTENDANCE AND PREPARATION (STAFF) OR STUDY (STUDENTS) FOR DIFFERENT KINDS OF SESSION

—	Seminar	Discussion	Practical	Demonstration
Students:				
Attendance (hr. per session) ..	1·25	1·5	2·0	1·5
Private study (hr. per student per week)	9·4	9·8	10·6	8·8
Staff:				
Attendance (hr. per session) ..	1·25	0	2·0 (×2)	1·5 (×2)
Preparation ,, ,, ..	0·5	1·0	1·0 (×2)	2·0
Technical and other assistance:				
Attendance (hr. per session) ..	0	0	2·0	1·5
Preparation ,, ,, ..	0	0	4·0	2·0

than from the other kinds of teaching. This is a possible explanation, and one that should be investigated. If the other methods really add nothing to lectures, they might well be abandoned. The necessary experiment is difficult (but not impossible) to arrange. At the moment practical classes and demonstrations are obligatory in most medical courses, although there is, as usual, no experimental evidence to justify such regulations.

Relative Economy of the Methods

54 of the 62 students completed records of the ways in which they had spent their working time.

These were full enough to present a picture that was consistent with their observed behaviour during the course. There was very little reported absenteeism from the official periods of teaching (22 absences in a total of 540 possible attendances, or about 4%) although the 8 students who did not hand in records may have been absent more often. The amount of time students spent in reading textbooks, other references, or their own notes ranged from 0 to 21 hours per student per week for the subject matter of this course alone, with a mean of 9·7 hours. About 2 out of every 3 students spent more time in reading their own notes than in reading books.

There were no systematic or significant differences between the 4 groups in the distribution of their time. The number of hours spent on private study did not correlate with the score in the final test ($r = 0{\cdot}02$), nor with the improvement in score during the course.

The average time spent by students and members of the staff in preparing and attending the various kinds of session is shown in table IV. As far as students are concerned, seminars and discussions were supported with very similar amounts of bookwork. Practicals, on the other hand, took up about 20% more time than did demonstrations. For teachers, too, practicals consumed about 20% more time than did demonstrations; and when the time contributed by technical staff is considered, the economy of demonstrations becomes striking. For teachers, discussions are much more economical than seminars. There is, therefore, a partial conflict between the interests of students and teachers.

Students' Attitudes to the Teaching Methods

The discussions of groups which used recordings seemed to be much more vigorous and extensive than were those of the seminars conducted by a teacher.

Students from the former groups returned, singly or in twos and threes, to listen again to the recordings more often than students from the seminars returned for further information or discussion. Students who attended the recorded sessions said that they found the material useful (particularly the factual sections), that they enjoyed being taught in this way, and that they felt their discussions of the points which they did not understand were freer in the absence of a teacher than they would otherwise have been. On the other hand, some students felt that the presence of a teacher would have provided a greater stimulus. It was also suggested that smaller groups would be still more enjoyable and successful. This would obviously be easier to arrange with the use of tape-recordings than with personally conducted seminars.

The teachers felt that in the opinion of the students the advantages of discussion groups over seminars outweighed the disadvantages. In practical classes, however, the advantages of small groups seemed to be outweighed by the satisfaction of "seeing things work properly" in demonstrations. These views were assessed more objectively at the end of the course by asking each student to award a mark (out of 10) to express (a) the use, and (b) the enjoyment he had derived from each method of teaching. The marks awarded are summarised by groups and methods in table v.

Lectures were considered by all groups to be outstandingly the most useful, and by 3 out of 4 to be the most enjoyable, method of teaching. Demonstrations followed some way behind, with seminars a close third and practicals a close fourth. Reading was thought to be almost as useful as practicals, but much less enjoyable. Discussions were rated a bad last for usefulness but were more enjoyable than reading.

Students who participated in discussions awarded a lower mark to the course as a whole for both usefulness and enjoyment. They gave particularly low marks for practicals and reading, as well as the discussions themselves. These methods all involved little contact with teachers, and dissatisfaction with a lack of such contact may be responsible for this, and for the below-average award for lectures (which are also relatively impersonal) and the high award for demonstrations (in which there is more contact). Differences between the groups taught by practical classes and demonstrations were smaller.

Care is needed in interpreting these results as an indication of a desire for more "positive" direction of their work, although this desire is well known in other educational contexts (Wispé 1953, Fox 1957). Still greater care is needed before the results are allowed to influence the choice between methods which encourage passive receptivity and active curiosity

TABLE V—STUDENTS' ASSESSMENT OF TEACHING METHODS

(U = usefulness; E = enjoyment; maximum marks = 10)

—	Lectures		Demonstrations		Practicals		Seminars		Discussions		Reading		Mean	
	U	E	U	E	U	E	U	E	U	E	U	E	U	E
Group:														
I	8·0	7·8	7·9	8·2					5·0	5·7	6·5	4·7	6·9	6·6
II	8·4	8·3			6·0	6·6			5·2	5·9	6·1	4·3	6·4	6·3
III	8·6	8·5	6·4	6·8			7·3	7·2			7·1	6·4	7·4	7·2
IV	8·6	8·4			7·5	6·4	6·6	6·8			6·9	5·8	7·4	6·8
Groups attending:														
Practicals	8·5	8·3			6·8	6·5	6·6	6·8	5·2	5·9	6·6	5·1	7·0	6·6
Demonstrations	8·4	8·2	7·0	7·4			7·3	7·2	5·0	5·7	6·9	5·6	7·1	7·0
Seminars	8·6	8·4	6·4	6·8	7·5	6·4	7·0	7·0			7·0	6·1	7·4	7·0
Discussions	8·2	8·0	7·9	8·2	6·0	6·6			5·1	5·8	6·3	4·5	6·7	6·4
Mean	8·6	8·4	7·0	7·4	6·8	6·5	7·0	7·0	5·1	5·8	6·7	5·4	7·1	6·8

(*Lancet* 1958). It is certainly relevant to inquire whether there is any relationship between the difference in the attitudes of groups taught by various means and in their test performances. Correlation of the total estimates of usefulness or of enjoyment, and final test marks in sections B, C, and D gives $r = -0{\cdot}22$. This is of doubtful statistical significance ($P \simeq 0{\cdot}1$) and too much must therefore not be made of the negative sign.

There is at least a suggestion that the more critical students perform better and the less critical less well. This relationship is not found in all circumstances (cf. Ash 1951, Wispé 1951, Smith 1955). Motivation would not really be expected to affect performance to any great extent in so short a time as that occupied by this course, but important interactions may occur over longer periods.

Discussions started by tape-recorders may be particularly useful when a shortage of teachers seriously limits the amount of instruction that can be given. Even when this is not so, additional teaching can be given in this way for smaller groups, or even for individuals, as Graves and Graves (1958) are doing for general practitioners.

As for the comparison of demonstrations and practical classes, the former usually "work", they are more efficient in that they require less time from teachers and students (who in any case prefer them), and they are not demonstrably less effective. The acquisition of a trivial amount of practical skill with laboratory animals is of doubtful advantage to a medical student, and it may be (as far as preclinical pharmacology at least is concerned) that practical classes could give way to more pleasant and effective ways of using the time. Our initial classification of teaching methods into "active" and "passive" therefore does not run parallel with any division into methods which are more useful or economical or enjoyable than others, but we have given experimental support for the belief that an active method (discussions) and a passive method (demonstrations) are more useful and more economical than their closest alternatives, when used in conjunction with lectures and reading.

Summary

Matched groups of preclinical students were taught about the pharmacology of the peripheral nervous system by means of lectures. In addition, each group attended either demonstrations or practical classes, and either conventional seminars or discussion meetings initiated by playing back recorded material, in the absence of a tutor.

The relative value of each method was assessed from the gain in knowledge (as tested by objective examinations), from the time spent by teachers in teaching and students in being taught, and from the students' own attitudes to the course.

The gains in knowledge did not differ significantly from one group to another.

Demonstrations were much more economical of time than practical classes for teachers, technicians, and students. Discussions required less time of teachers than seminars, and the corresponding difference for students was very slight.

Students thought demonstrations more enjoyable and more useful than practical classes, and they valued seminars more highly than discussions.

The amount of time spent by students in private study showed no correlation with their test scores.

We are grateful to our students for their continued encouragement and criticism.

References at foot of next column

The Wider World

ISRAEL

The Evolution of an Idea

HEDY SYMONDS
M.D. Vienna, M.R.C.S.
LATELY CHILD PSYCHIATRIST, WORKERS' SICK FUND, AND DIRECTOR OF THE MENTAL HEALTH CLINIC, ICHUD HAKIBUTZIM, ISRAEL

(*Concluded from p. 513*)*

THE CITIES AND THE SETTLEMENTS

THE three big cities of Israel show much variety.

Jerusalem I had to visit some ten times in almost as many years before I understood its symbolical significance. The road winds and curves through vineyards, reconstituted ancient terraces, and soil-eroded hills which now again bear the marks of cultivation. There are pencil-slim self-contained cypresses, spreading larches, and fir trees grown to forests as one climbs up to 2400 feet. The glimpse of the old city, which is all one can get now, shows it to be a small enclosed town on the top of a hill. Just as the road leading up to it is alive with hard labour, the outgoing route is barren of any vegetation and leads to the Dead Sea. Thus Jerusalem stood in men's minds as the highest point life may reach before its decline to death.

It is extremely interesting that the new Jerusalem, on the opposite hills, is Israel's most successful combination of geographical and architectural planning.

Tel-Aviv struck me at first—nine years ago—as an ugly city, where individuality has run riot and styles are inharmoniously mixed. On further enforced acquaintance I have come to think of her as a plain woman whose vitality, tolerance, and general sensitivity endear her and make one forget her looks. Not only has much happened which indicates an inherent striving for beauty, but she has life with abandon—vibrating, responsive, enjoyable, and keenly controversial. The open-air cafes, the seashore with its strollers, the street vendors and stationary booths, the breathtaking beauty of massed flowers on barrows at street corners, and the activity at all hours of day and night are a permanent attraction.

Haifa is a truly beautiful woman, but if she has a soul she keeps it hidden from prying eyes. The location is superb: Mount Carmel overlooking the bay; in the background soft hills, reflecting pink, blue, and grey light, and often shrouded in mist. At night, with the lights twinkling over what seem great distances and many depths, it is like fairyland. The planning of the city, if not the excessive uniformity of its architecture, is far superior to Tel-Aviv; yet the feeling it gives is of a town asleep.

The agricultural settlements, or *kibutzim*, are Israel's most distinctive feature. Some sixty years ago the first were started by pioneers of the most devoted kind. From a trickle they became a stream; and the official policy of returning to the land became a characteristic of the Jewish revival. By the end of the first world war, influenced by the revolutions in Europe, and especially in Russia, the ideology of the kibutz had crystallised

* In the first part of this article two important words were transposed. The first sentence of the fourth paragraph in column 2 on p. 511 should say that "throughout the Old Testament *subjective* truth always takes second place to the *objective*".

DR. JOYCE, PROF. WEATHERALL: REFERENCES

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and embodied the most exacting communist ideal. Its members received no payment or reward of any kind, nor much privacy, but lived as communities under conditions of hardship, danger, and privation of many sorts.

The unconscious motivation of action, under the guise of rational tenets and objective needs, can nowhere be more apparent than in these efforts. The members of the kibutz, having been intellectuals and comfortably off, became peasants and penniless. Nurtured on anxious parental love, their ideal became the impersonal hygienic care of children in separate children's houses. From the generations of townbred and confined people, the independent and daring *chalutzim* were born.

This was a revolt, in the setting of the general post-war revolt in Europe, but again specifically Jewish. It was a revolt against, among other things, the Jewish fate. It carried the Jewish intensity to the opposite extreme. When the Russians, Italians, or Germans felt it necessary to worship the new gods of rationality and science, they retained their right to a private emotional life. To the Jews of the kibutzim it seemed necessary to share all their possessions, their emotions included. This implied a conviction that reason can rule over instinct. From what we know of human nature, this experiment was bound to succeed for a time and in a way, just as it was bound to fail by not taking account of human weaknesses. That humans must, in the long run, express personal preferences and intolerance, and that every community must have outlets for these, was denied in this utopian drive.

Whereas in Europe in the 1920s emotional disillusionment gave rise to dictatorships which were rational only in their superstructure and used their emotional impetus for coercion and crusades of hate, in the Jewish kibutz the aggression was used partly against the external environment (so that arid and eroded fields were made fertile) and partly in censorship of the individual. The demand that all members of the community should fit into a rationally prescribed pattern bore so heavily upon them that, had it not been modified, a further complete change would have been inevitable.

Though the settlements retain the main tenets of their founders, a gradual change in their ideology has shown how sensitively they respond to general trends discernible elsewhere. Some 200 in number, they now allow their members private homes, some personal possessions, and holidays. Parents now take a much more intimate interest in the upbringing of their children and can make their own choice in diverse matters. Meals are still taken in communal diningrooms, and the children continue to live in separate homes, under the care of trained personnel; but further steps towards re-establishment of a family pattern are frequently and hotly discussed.

To live in such close proximity with others imposes strain and increases the difficulties of emotional relationships. The continuous watchfulness of the parent is replaced by the watchfulness of the community over its members. In turn, the community receives the resentment a child feels towards its parents, and much dissatisfaction arising out of personal demands and deficiencies is put down solely to the conditions under which the members live. Tensions are worked out partly through vocal demand and modification of procedure (the most rational approach), partly through going away (which leaves mutual ill-feeling), and partly through help with emotional problems, leading to better understanding. The community framework is particularly helpful to many who, in a more competitive atmosphere, could not be useful citizens.

The cultural activities are on an unexpectedly high level.

Every kibutz (the saying goes) has at least one enthusiast; and, thanks to such a person, one in the north has excavated a Byzantine temple and now houses a museum with mosaics, pottery, Phœnician glass, coins, and other archæological remains of remarkable richness. Another, on the shores of Lake Tiberias, has built a concert hall seating 2000.

One of my most surprising experiences concerned this hall. To attend a concert at Easter—a yearly feature—meant crossing the lake by boat. Having other boat trips in mind, I was expecting lights, gay crowds, and a festive atmosphere; but instead we embarked in total darkness. A police boat accompanied us to give protection from the Syrian shore, and sinister searchlights were the only reminders of the lights of a pleasure trip.

Most of the settlements are near the borders, and preparedness for attack is the keynote of their days. While contributing to consolidation, this adds another strain to those of a more personal nature.

THE YOUTH

Every country has conspicuous features on which comment by new arrivals becomes hackneyed. (Nowadays even a visiting film-star will avoid mentioning the London policeman.) Ever since people have come to Israel they have been making the same astonished remarks about the children.

Again and again one is struck by their vitality, their independence, and their unlikeness to Jewish children elsewhere. Most of them are fair; all are well grown, tough, and confident-looking. They wear bright colours; and seeing a group of them in animated discussion out of doors—their cardigans tied round the waist, their hair flying in the wind—one cannot but admire. How far this remarkable physical fitness and independence are simply the result of expansion in a free atmosphere it would be hard to say; but certainly they are fostered by every available means. We know that parents pass on their anxieties and frustrations to their children at an early age; and in Israel, more than elsewhere, parents have reason to be anxious and frustrated. Here, as in other countries, suffering and error militate against the best conscious intentions; and we should expect the intensity and the narrowness of the early relationship to have the same consequences as everywhere else. In my own work I have found this expectation amply justified, for I deal with psychological problems. The reasonable conclusion seemed to be that, whereas physical deficiencies can be rectified in one generation, psychological ones must take several.

Yet, though psychological problems are as common as in Europe, there is a difference. One is reminded of Freud's saying that the long-term effect of the early parent-child relationship is particularly great in the European culture and is considerably modified in more permissive social environments.

The importance of later experiences is amply demonstrated by the change seen during school years, producing different behaviour patterns in adolescents. In Israel from about 8 years of age all children belong to youth organisations, go on strenuous excursions (led by a boy or girl only 2–3 years older), and pass endurance tests which anywhere else would be thought excessive.

Free time, especially the eve of Sabbath, is spent in groups, where a choice of companions, challenge, and group support enable the youngster to test objective reality afresh. The response of the group is not as predictable as the response of the home, and through these experiences the child gains a new picture of his own abilities. His unconscious relationships with his parents may be considerably modified.

It is here, I think, that Israel may be making one of its biggest contributions. As a preparation for future personal relationships, our Western society is neither consciously planned nor unconsciously successful. We know that the child, passing from the security of the home, requires another type of identification—namely, with the society of which he is a member. At first the Israeli group represents greater physical freedom, but by adolescence it gives greater emotional freedom as well. The child is supported by a larger framework, in which there is wide choice of friends of both sexes and the limitations are acceptable because they are imposed by people he admires. This transition from home to a modified independence, with censure and support, seems an admirable route to the still greater independence required of the young adult. In his inevitable revolt from the parental home, the adolescent thus finds new ready-made channels in which to test his capacities, attach his longings, and rectify the distorted pictures formed by infantile fantasies.

The results of this new type of living are visible everywhere in Israel. Early marriages—the result of stable adolescent relationships—are the rule, and the offspring are free from much of the insecurity and anxiety of previous generations.

THE SIGNIFICANCE OF ISRAEL

Because of their peculiar position, the Jews have always been hypersensitive to the environment, to which (compared with members of securely established nations) they feel exposed. This sensitivity, developed through generations, has often led to the sensing of trends of thought before these were recognised: thus Marx in the economic, Freud in the emotional, and Einstein in the scientific fields broke fresh ground. National revival was another new departure in which the Jews were pioneers at the end of the 19th century.

The point of unity for Jewish nationalism was religion, which I would define as an expression of the emotional and irrational components of human nature—its aspirations and fears. Science, on the other hand, is an expression of the rational and tangible; and, because human beings contain both these elements, there is a continual striving to bring one into line with the other. In the second half of the 19th century scientific inquiry and religious doubt could and did flourish in an atmosphere of almost universal belief. The attacks made on established religion by a minority could be tolerated because this established religion had enough security not to become openly oppressive. Scientific findings discredited more and more of official religious tenets. Then came the tremendous anticlimax, the emotional disillusionment of the first world war. It tilted the balance towards the scientific attitude and one which conflicted with established religious practice.

Between the wars, the dictatorships, whether of the Left or the Right, discarded official religion and turned to scientific advances as likely to produce millennia of bliss. Each contained a creed disguised as rational, and their extolling and practice of science added new striking-power to the underlying negative human emotions. Intolerance, hatred, and violence were given opportunities they were formerly denied.

One reason for the apparent return to religion—official religion—in the United States and Britain is the belief that religion was the force that prevented creation of materialistic dictatorships in these two countries, and that morality's tenuous hold on humans cannot be strengthened, and emotional satisfaction gained, except through accepted forms of religious adherence. This particular attempt at reconciling the rational and scientific with the irrational and subjective is as yet in its infancy. But the force of conviction is lacking; the religious revival sits uneasily even on official functions, nor is it successfully accomplished in the individual.

As one might expect, this crisis of religion is even more evident in Israel, a State explicitly founded on religious unity. Most immigrants from European countries have long since lost most of their faith in religion as such; but there are a militant minority who want to re-establish the conditions under which they formerly lived—to create a spiritual ghetto. Just as they have remained undisturbed by the sceptical trends of the 19th and 20th centuries, they are unaffected by the spirit of our times. Free from intellectual doubt, they can act with the emotional conviction of crusaders. They are the more vociferous equivalent of those who, in other lands, can see only outworn forms as answering present needs.

In considering this conflict, we must remember that the Jews always had a father, and that the only security they have known is of a moral kind. Coming to Israel, the Jewish equivalent of a sophisticated European has found himself in a situation where his intense longing for identification—the anxiety and the fear—formerly attached to religion has a new object. While attaching his emotions to his country and tackling its tasks with religious intensity, he is left unsatisfied by the gods of science, though he knows that they alone can bring material salvation. May not the Jews, as specialists in evolving moral codes, find means of living ethically, while discarding religion, or recasting it in a new form?

It is in this reconciliation of emotional and physical needs that Israel is making her second important contribution to the contemporary scene. In dozens of different ways a modus vivendi is being found, emotionally satisfying yet not offensive to reason.

The Sabbath is celebrated emotionally, expansively, but not by going to the synagogue. Flowers, clean clothes, a festive atmosphere, restraint from work, but active enjoyment of the sea, give that day a holy, yet wholly enjoyable, aspect. The kibutzim, the most organised and most sensitive organs of community life, produce each religious festival with a deep, ageless, emotional content but unattached to any deity.

I attended a harvest festival at such a kibutz. To an amphitheatre, made of blocks of pressed hay, with an altar of the same material, people of all ages came in gay attire and expectant mood. The children, in groups, with garlands on their heads and flowered hoops in their hands, were the first to dance. Then came the older children, in flowing Grecian robes, who as they ended their dances placed their sheaves upon the altar. Adults brought examples of everything the settlement produces, depositing it with reverence and gratitude, and thereby acknowledging a human longing to give thanks. To whom, or to what, was left to the imagination.

Thus we see the trend towards recognising innate irrational human needs, which neither require nor repudiate scientific proof. One prerequisite for this attitude is a belief that the strength that a people needs for living ethically comes from within, not from professing an official religion. Another is that neither science alone, nor the emotions alone, can direct our lives satisfactorily. Too much repression or disregard of the emotions produces personal unhappiness and national disaster; but, given a suitable outlet, they need not interfere with our exercise of reason.

When we reflect that this experiment in nationhood, which does give an outlet both to religion and rationality, is being carried out by a mixture of people from 70 nations, whose experiences often match in violence and suffering the worst that fantasy could envisage, we must find reason for hope that the world as a whole—70 nations and more—will be able to heal its present divisions. The degree of success attained seems to justify our belief that recognition of emotional needs, and their acceptance, leads to a wisdom and tolerance more mature than that of earlier ages because it does not rest on a spurious belief in goodness or on denial of the bad.

An experiment in miniature, Israel shows how people of different cultures, expectations, and temperament can be united through an idea. The world's greatest need is for the resolution of conflicts in an atmosphere of readiness for experiment and the toleration of differences. Both our emotional and our rational components have to be accepted before our lives can be either as satisfying or as progressive as we all wish. Israel's role is important as a sensitive exponent of trends existing everywhere.

Public Health

Influenza

DEATHS from influenza in England and Wales in the week ended Feb. 28 numbered 1571, compared with 1121 in the previous week. Of the 1571 deaths, 1120 were of patients over 65 years of age. The increase in deaths was less steep than in the previous week; and, according to the Ministry of Health, there are indications that winter illness reached its peak in the second half of February. Pressure on hospital beds has eased in London, Birmingham, and Manchester. Influenza remains widespread; but the distribution is patchy, and some areas have largely escaped infection.

Infectious Diseases in England and Wales

Disease	Week ended February			
	7	14	21	28*
Diphtheria	2	5	2	5
Dysentery	1294	1346	1193	1049
Encephalitis:				
Infective	2	3	3	1
Post-infectious	1	2	13	5
Food-poisoning	129	125	107	148
Measles, excluding rubella	22,170	25,196	26,493	24,951
Meningococcal infection	28	30	27	35
Ophthalmia neonatorum	29	24	19	29
Paratyphoid fever	10	3	6	11
Pneumonia, primary or influenzal	943	1465	2339	2926
Poliomyelitis:				
Paralytic	12	11	10	7
Non-paralytic	6	..	2	2
Puerperal pyrexia	218	237	265	309
Scarlet fever	1389	1218	1247	1207
Smallpox	..	..	..	..
Tuberculosis:				
Respiratory	504	457	462	476
Meninges and C.N.S.	2	5	4	6
Other	45	45	43	47
Typhoid fever	..	2	4	2
Whooping-cough	758	789	575	589

* Not including late returns.

In England Now

A Running Commentary by Peripatetic Correspondents

MY interest in the clinical thermometer goes back to 1920 when I first beheld its inventor, Sir Clifford Allbutt. He was then a septuagenarian but still rode his tricycle through Cambridge. He was always immaculately dressed in his morning coat, grey waistcoat, striped trousers, spats, white gloves, and, if I remember correctly, a Homburg hat. For some twenty years I have used the ordinary thermometer which goes from 95° to 110°; in the past five years I have used the "premature" thermometer which starts at 90° and I know that if it has risen to 97° the patient has not got a fever. But this week I had a new experience. A patient, a farmer's wife, said her fever was like a horse in the morning and a sheep in the evening. She had borrowed her husband's veterinary thermometer which has on one side:

	Man	*Horse*	*Cow*	*Pig*	*Sheep*	*Fowl*
The normal temperatures of these animals are ..	98[4]	100[2]	101[4]	102[4]	104	107

Below Cow, are Dog and Cat which have the same normal. As a farmer's son, I have always taken some interest in comparative medicine, but I did not realise the wide range of normal temperatures.

* * *

It started after I had seen an eminent neurologist on the telly. With a foppish flick of the wrist, using a little rubber-tyred wheel on a length of cane, he produced one casual jerk after another from the limbs of his recumbent patient. I was astounded. Years of beating patients with the side of my hand had produced only bruises. I needed an instrument like that. So having removed one of the rubber-tyred wheels from my son's latest red toy tractor I was screwing it on to a length of cane when the owner of the tractor caught me. I had to put the wheel back of course, but when I had nervously explained what I had been hoping to make, his attitude softened. He would help to equip me like the Great Man. He would make a jerk hammer for me.

He kept his word. It was finished the next day and placed lovingly on my desk. Or more accurately it was leaning against my desk, being a little too big to lay on it, consisting as it did of one solid-tyre back tricycle wheel, $1^1/_2$ ft. in diameter, lashed with wire to a 6-ft. chestnut paling. It lay there like the surviving ski stick of some drunken Scandinavian giant come to a nasty end in the downhill slalom.

The first Thor-type jerk hammer! As I looked at it I began to wonder, was he perhaps not on to something? Never have we doctors been so decadent as today. All dripping with the milk of human kindness. Drowning our patients in it. Tablet for your headache, balm for your sprain, a lozenge for the sore throat. With a Thor hammer we could breed a new virile muscular race of doctors, swinging lustily from one reflex to the next, from whose thunderous blows the most tabetic of knee-jerks would not be safe. And so on to a new Golden Age, where the doctors would once more be healthier than the patients.

* * *

Marriage to a pædiatrician has many drawbacks, chief of these are his pædiatric samples. Pharmaceutical firms are far too generous in their offerings of antibiotics and other drugs carefully flavoured for the infant palate. Though my year-old child relishes their cherry or raspberry flavour, I do not. Of course I quite understand that it would be wasteful and extravagant to buy any of these medicines when the surgery drawers are overflowing with the identical thing; but I sometimes gaze darkly at the slumbering form of my husband as I awake 6-hourly to consume vast quantities of banana-flavoured, sticky substances.

* * *

Doctors are often charged with extravagance in prescribing, but we have found that, if you look in the right shop, substitutes can sometimes be found for expensive drugs.

Rebecca is one of those pale, elderly rheumatoids who readily become perpetual patients. Her rather sad, slightly

oval face has dogged our clinics for years, but the complaining never became any less. Her moderate deformity is obvious but not progressive. A couple of years ago one of the physicians, overcome by her continual lamentations, and with the justification of a persistently elevated E.S.R., started a course of prednisolone. Since then the efforts of all have been devoted to reducing the dose. All, that is, except Rebecca who developed a critical dose-level below which complaints were renewed.

At her last visit Rebecca's joy was obvious from afar. She now needed only a quarter of her former dose, since she had discovered for herself a new and effective liniment for her wrists and hands. Coyly she explained that her interest had first been roused by an advertisement in a cycle shop and she produced a tin of rust-remover. LUSOL loosens JOINTS and NUTS.

* * *

Lister and his theories have been loyally accepted in Glasgow ever since Edinburgh, in a television advertisement, sought to convey that his great work was really Edinburgh stuff. True he went to Edinburgh, after his heart and spirit were broken by Glasgow resistance, but he fared so badly there that he was driven to London. There, of course and inevitably, he fled to retirement. From there his fame spread backward to the medical schools. Is there a lesson here?

* * *

Nowadays my patients announce *their* diagnosis—viz., "I have sunspots"; "I've got one of them blood-groups that's going about". More technical are the extramural students at the T.V. School of Medicine who usually arrive at a diagnosis at 2 A.M. "You needn't try to kid me, Doc.—it's pilonidal cystophrenia, isn't it? I give myself six weeks and I've left my body to St. Ledger's . . ." Or "I appear to have a typical Leberwurst-Bürp syndrome. I know that this is purely academic but please arrange for in-vacuo estimations of my intracellular detritus."

The counter to this goes roughly as follows: "The Herren Profs. Leberwurst and Bürp (personal communication) now believe that the significant factor is the ratio of intra- to extracellular detritus, which must initially be stabilised by a six-week course of treatment with the following mixture." This is where you prescribe whatever *Mist. diabolicas* you can think up at 2 A.M. For masochistic patients who might enjoy the above regime, announce that detritus estimations involve biological assay using serum from almost any creature you can remember which (if not extinct) is rare, ferocious, and the hell of a long way off. (I favour king cobras, cœlacanths, giant squids, and Abominable Snowmen—in that order.) Add casually that the patient must, of course, provide these little luxuries for himself, and express your readiness to sign his passport photograph.

* * *

In the beginning the Creator made the doctor. He made him generous and jealous, logical and inexact, faithful and cynical.

On the second day He created the Bacteria and said: "The hæmolytic streptococci shall destroy the people but the non-hæmolytic ones shall pass them by as the breeze over the waving corn, and the non-lactose-fermenters shall be a scourge on the innocents but the lactose fermenters shall be the strength of their digestions."

On the third day He created the Vitamins and Hormones and said: "Behold, the Vitamins and Hormones, how they toil. They toil in the bright rays of the sun and in the dark folds of the seed and woe unto him that hath them not."

On the fourth day He created the Antibiotics and said: "This shall be a sign for you, a universal remedy, infallible, invincible." But Resistance thwarted them.

On the fifth day He created the Psychotherapists and said: "I leave it to you." And they arose and built themselves little temples and the people lay down and worshipped them.

On the sixth day He created the Will-to-Live and said: "Let the patient live."

On the seventh day He looked on His handiwork and saw that every good had an antagonist and every ill had an antidote and every antidote had a neutraliser. He was satisfied that none would win or lose and that all would live and die.

Letters to the Editor

MENTAL HEALTH BILL

SIR,—The Bill's arrangements for psychopaths are bewildering.

First there is the definition that those who can be detained for treatment under this heading "require or are susceptible to medical treatment". Though many would subscribe to the view that psychopaths *require* treatment, how many would say that they are susceptible to it, especially *medical* treatment using the term in its accepted sense? Except in a unit such as Maxwell Jones', staffed by specially picked and largely dedicated personnel, so much "treatment" is disciplinary training. Yet by definition hitherto psychopaths have usually been regarded as the hard core of people who do not respond to either treatment or punishment. If in future they are to be detained in hospital, then the power of discharge which can now be exercised is lost. What then is to be done with the unruly psychopath who will not conform? Presumably he will have to be docked of his privileges. This he will not like, and the next step must be to confine him to a ward. Is there to be a special closed ward for psychopaths? Or do they go in with the unpredictable psychotics?

If psychopaths are to be involuntarily detained, the necessary facilities will have to be provided. At present the theoretical safeguard for hospitals is that they need not accept a patient unless that patient is willing. But if a sufficient number of psychopaths are unwilling, hospitals will surely be directed to take them, or at any rate strong pressure put on the superintendent; after which the consultant in charge of the case, who has had no say in the admission, will have to cope with his unwanted and unwilling charge. A very important consideration in all this is that aggressive psychopaths are not exactly *persona grata* amongst other patients, and their admission in any number may well set the clock back in the public's attitude to psychiatric hospitals.

If I thus speak unsympathetically of psychopaths, I also want to defend them. They are to be detained because of their aggressive behaviour, in their own interests, or because they are dangerous to society—not because they are insane. Yet this deprivation of personal liberty is to be made on purely medical recommendation on what are really sociological grounds. Though, like many doctors, I have felt annoyance when judges would not take my advice, I think the courts are right in objecting to trial by psychiatrist. Yet this is what is to happen to sufficiently turbulent young people. It is true that there is an appeal to a tribunal, but on the whole it is always easier to get in than get out. It seems to me undesirable that a doctor should ever act as a judicial functionary; but as regards psychopaths there is a particularly strong case for a judicial order, and for a special panel of suitably experienced legal functionaries whose duty it would be to make the order.

Finally certain other considerations arise. The definition of psychopaths requires them to be aggressive; hence drug addicts, who badly need forcible detention to try and cure them, escape. And what of recidivist sexual offenders, where punishment is useless and often cruel? Will the homosexual go to prison, while the young man with a flick-knife has the benefits of hospital? What is needed are special institutions to which all such cases can go; but the ordinary psychiatric hospital is not the place for them.

London, W.1. W. LINDESAY NEUSTATTER.

SIR,—Almost all commentators on the Bill have emphasised that its implementation will require a large number of additional psychiatrists. If these are to be forthcoming it will be necessary for the status both of psychiatry and of the consultant psychiatrist to be raised to a level concomitant with that of general hospitals.

One of the principal factors handicapping the progress of clinical psychiatry is the medical administrative structure, and that this needs a complete reorientation can hardly be doubted after reading the correspondence you have published. A second very important factor is the lack of information about numbers of extra medical staff needed in mental hospitals, and this is at present being investigated by a subcommittee of the Royal Medico-Psychological Association.

At a recent meeting of the Surrey Inter-Hospital Psychiatric Association, the medical staffing structure of the mental hospitals represented was discussed, and it was felt that some of the provisional conclusions merited a wider circulation.

As a basic principle it was unanimously agreed that the medical staff should be divided into teams of four, consisting of a consultant, a senior psychiatrist of S.H.M.O. or senior-registrar status, and two medical officers of junior status. Each team should be responsible for 400 beds, in addition to which they should devote a proportion of their time to outpatient and allied work. But in view of the increasing need for the latter it was calculated that the hospital would need two additional psychiatrists for every quarter of a million population catered for.

These quantitative estimates for medical staff have been brought forward now in order to stimulate thinking on this matter. A policy for our specialty will soon have to be formulated.

A. J. OLDHAM
Hon. Secretary,
Surrey Inter-Hospital Psychiatric Association.

St. Olaves Hospital,
London, S.E.16.

SIR,—Dr. J. T. Hutchinson (Feb. 28) charges the Royal Medico-Psychological Association and the British Medical Association with failure to give a lead to the Government about mental hospital administration, and failure to recognise that times have changed. By exhorting these bodies to statesmanship he implies a shortcoming in this sphere also.

The Royal Medico-Psychological Association submitted evidence to the Royal Commission, and most of its recommendations were embodied in the Commission's report, and later in the Bill. Why, then, does Dr. Hutchinson deny credit to the Royal Medico-Psychological Association for helping to produce a Bill which he describes as "excellent"? The Association recognises that the question of mental hospital administration is wider than the immediate issues raised by the Bill. It has therefore formulated a policy on the topic and has forwarded its views to the Government. These activities, and others which space precludes me from mentioning, surely constitute "giving a lead".

Dr. Hutchinson seems to link his charge of failure to recognise that times have changed with a suggestion that the Royal Medico-Psychological Association wishes to maintain a system of patriarchal superintendents. This is difficult to reconcile with the Association's emphatic repudiation of the concept of the superintendent as an autocratic boss, or with their care in emphasising that the definition of the "responsible medical officer" should be phrased to indicate that the person meant by it is the psychiatric consultant in charge of the case.

It would not be seemly for the Royal Medico-Psychological Association to claim that its policy is statesmanlike. Nevertheless it has a policy which recommends steering a course between the extremes of maintaining the status quo and abolishing superintendents altogether. Any discussion as to whether this policy is statesmanlike must revolve round the facts, not around misconceptions. The Association recognises that, in a fast-moving situation like that presented by the Bill, the ordinary channels for disseminating information may operate too slowly. Any person with a bona-fide interest may, however, obtain authoritative and up-to-date information by applying to the office of the Royal Medico-Psychological Association.

Royal Medico-Psychological Association,
11, Chandos Street,
London, W.1.

A. B. MONRO
Hon. General Secretary.

SIR,—I am glad that there were no serious objections to my letter of Feb. 7. Such minor criticisms as there were have their answers, as your thoughtful readers know. Mental hospitals are not general hospitals, and whatever they are called they never can be. I can see some point in a general hospital having a medical superintendent—there is all too often a need for someone to care for the lost outpatient, to complain about the food and the extraordinary hours the patients keep, to help the inconvenient visitor, and to cherish the "silly" patient who gets frightened and makes a fuss. But I hesitate before considering a mental hospital without one; it would be like a body which lacked not only a heart but also a head.

Some of us medical superintendents are oldfashioned and do silly things, but we can learn. Some of us may be unreasonable terrors (perhaps no worse than our colleague the administrator officer); but even at our worst we are insignificant beside the worst of our predecessors, and I have never heard a serious complaint of the youngest of our race. I very much doubt if any younger medical superintendents have any wish to limit their consultant colleagues' responsibilities; the junior members of the medical staff get much greater responsibility than their opposite numbers in general medicine, and indeed are more likely to complain that they are given too much rather than the other way round.

The chairman of a medical staff committee elected by the doctors is bound to change, and I think that hospital management committees and regional hospital boards prefer to deal with a person who was in office when a scheme was first mooted two years earlier and will still be there when it comes to completion in three years' time. If a hospital is to have a policy of development instead of a series of plans, it requires one medical man in charge for many years.

There are so many insignificant-looking things which are tedious and contribute little to the personal relationship between doctor and patient and yet make all the difference to every patient's comfort, and which should perhaps be the responsibility of every doctor. But what is the duty of many tends to become the care of none, each thinking that the others have attended to them; so a medical superintendent seems to be a necessity.

In a short letter it is hard to describe a philosophy of medical administration; but fundamentally what is needed in a mental hospital is a happy partnership between doctor, nurse, and lay administrator, with the doctor having the casting vote. I shall be surprised if anyone can raise any valid objection to this.

De La Pole Hospital,
Willerby,
East Yorkshire.

J. A. R. BICKFORD.

SIR,—There is no need, surely, for psychoanalytic formulations ("Analyst", Feb. 28) to explain the efforts of consultant psychiatrists to ensure themselves clinical autonomy. The disadvantages of individual power were epitomised more effectively by Lord Acton long ago.

There are dangers in concentrating the power of liberty and of discharge in the hands of one person.

Annual recertification is a doubtful safeguard, for few magistrates are in position to override medical evidence where it favours certification. The future of a number of patients on indeterminate sentence (certification) may therefore depend upon one [1] or another [2] optimistic or pessimistic assessment of the danger of, for instance, defectives to the community. It is even possible to look at figures for post-discharge success in two different ways. Thus Dr. Heaton-Ward (Feb. 21) thought my earlier figure of 76% successes with discharges distinctly unsatisfactory.

In my opinion power should be distributed by defining the " responsible medical officer " as one of consultant (possibly also S.H.M.O.) rank. In this day and age where 80% of patients are voluntary, superintendents could also be relieved of administrative responsibilities possibly better carried out by those who are trained for the purpose, leaving them free for the consultant work for which they also have been trained. The superintendent would thereby be relieved of the danger of losing his post, as I believe recently happened in one English region, because of administrative derelictions by a distant department head. Now that department heads are regarded as responsible to their own respective subcommittees, the superintendent is cast in the role of senior consultant to the hospital management committee, and his views are listened to with the respect they deserve as those of the principal representative of the medico-nursing team. It would perhaps be better if his position was defined as such.

Balderton Hospital, Newark, Notts. MICHAEL CRAFT Medical Superintendent.

SIR,—Those who have followed the correspondence about the difficulties of mental-hospital administration must think that some psychiatrists are rather an odd lot. To those of simple faith it might at one time have seemed that the subject matter of psychiatry was such that psychiatrists should be experts in interpersonal relationships; or at least that they should be able to get along with one another. It should in theory be possible to extend the idea of the therapeutic community in a mental hospital to include the staff.

Such simple faith is shattered by the revelations of your correspondents. The cynic has said that only the High Priest knows how empty the Holy of Holies is; but in this present context the psychiatric High Priests reveal that so far from being just empty the mental-hospital sanctum is full of devils. Or rather, of a devil in the shape and office of the medical superintendent. But the removal of medical superintendents does not get over all the difficulties. I would, therefore, support Dr. Hutchinson's plea (Feb. 28) for an inquiry into the form of mental-hospital administration which is likely to be most helpful in the future. The whole question of medical and/or lay administration has implications and complications beyond the boundaries of even the most disturbed mental hospital. Questions have been asked which have to be answered throughout the whole of the National Health Service, as witness the publications of the Acton Society Trust.

Perhaps there was at one time something to be said for the idea of a medical superintendent—to be responsible for the general wellbeing of the hospital, and to try to resolve rather than to foster the difficulties not only of the patients but also of the staff. In some parts this still works moderately well, in others it obviously does not work at all. Your correspondents have made it clear that there is much to be said against medical superintendents; equally that similar criticism may attach to chairmen of medical advisory committees, and no less to the idea of purely lay administrators.

The trouble is that whatever system of creative or co-operative leadership is evolved it will hardly be any better than the people who run it; which takes one back to the practical implications of the first paragraph of this letter.

Bootham Park, York. ARTHUR BOWEN.

SIR,—So far dispute mistakenly rages around the personality of the administrator. Shall it be a medical superintendent or the chairman of the medical advisory committee? Shall it be medical or lay? But these are not the crucial issues. The key question is should administration be absolutist, with some *one* exercising overall paramount authority, or should it be consultative with due measure of responsibility acceded to each job in its own right?

The basic minimum required of administration is *coordination*. This coordination should be not only vertical in a hierarchical sense, but also horizontal so that the administrator does not waste time in settling matters that can be quite simply smoothed out by the people immediately concerned. Not every issue requires a judgment from on top; within certain limits discretionary power can be extended to any link in the administrative chain.

Leadership is not necessarily attached to every administrator all the time; opportunities for leadership should be available at every level, and the function of administration is to draw out this potential leadership. That is to say, the concept of " shifting " leadership should be recognised. Without it the administrator remains inaccessible and cannot bring himself to admit or correct error, and regards new ideas as disguised shafts of criticism aimed at him—for not having thought of them himself. This feeds the myth created by the administrator that it is " lonely on top ". If it is, this is only because he has cut himself off from communication for fear of implied criticism.

Hitherto speculation has centred round the personality traits that make for a good administrator. This is a pastime for parlour psychologists and for sports writers trying to figure out why some football teams do better than others and decide that it is nothing to do with the footballers and everything to do with the manager. Administration has to do with the needs of the led; satisfaction of such needs is the most substantial test of successful administration. To satisfy the needs of the led the administrator must consult the led. This above all is what the authoritarian superintendent—medical or lay—cannot bring himself to do. For this reason hospital administration has lagged behind every other, for nowhere else has the administrator " paramount " authority.

In future, medical men had better strive to exercise influence rather than power. Power does not properly belong to top management; power may be necessary in the second, third, and lower levels of administration. Top management is concerned with policy not power.

If it is feared that the chairman of the medical advisory committee might become autocratic, obstinate, and inaccessible, then one has the comfort of knowing that he need not be re-elected next year. Alternatively the task of medical coordination could be taken in rotation.

Hitherto the best psychiatrists have looked to administrative jobs as a fulfilment of their professional aspirations, probably because the existing pattern of hospital administration did not permit any scope for the introduction of new ideas. But under the new Bill a consultant with full clinical responsibility, and autonomy for the team, would be given all the scope he needed and yet be held within the framework of clinical work interpreted in its bedside (or couchside) sense.

So far as training in administrative method is concerned, the orientation should be away from administration regarded as an exercise in a personally ambitious extension of the ego and towards the notion of administration as *social work*—its aim being satisfaction of the needs of the led.

1. Nelson, M. P. *Lancet*, Jan. 24, 1959, p. 201.
2. Hilliard, L. T. *Brit. med. J.* 1954, i, 1372.

Those who wish to retain the status quo should come out into the open and defend the thesis that " paramount " authority is necessary in medical administration. The defenders of the present faith unfortunately dominate the committees of the professional bodies which speak for the psychiatric lobby. The medical superintendents form the overwhelming majority of such committees and councils, and do not normally envisage their responsibility as including representation of contending " minority " views.

Chester. I. FROST.

WHOSE RESPONSIBILITY?

SIR,—Your leading article of Feb. 28 raises important issues.

No-one could doubt that the moral responsibility remains with the doctor, and had the editorial borne this title no exception could have been taken to it. In these days of legal aid the administrative responsibility should be made equally clear.

" Cross-infections " are due as much to overcrowding in busy wards, and to misuse of antibiotics, as to faulty technique on the part of surgeons. The cavalier attitude attributed to surgeons is surely the exception rather than the rule, and it should, in fairness, be mentioned that many advances in theatre and ward asepsis and antisepsis have been instituted by surgeons.

The committee system is indeed a necessary adjunct to the spending of public money in a democracy. One of the less desirable effects of this requisite of the National Health Service has been the decrease in the authority of the doctor, and the elimination of his executive responsibility.

The only course open to individuals in the face of overcrowding, antiquated facilities and equipment, and inadequate nursing and ancillary staff is to complain, and to continue to do the best they can for the greatest number under the circumstances.

Responsibility for the serious situation underlying the comments in your editorial is indeed widespread: the administrative set-up which accepts the executive responsibility, the medical profession as a whole, and even the contemporary medical journals—as well as stimulating us to greater efforts—must accept their share of the moral responsibility.

Oxford. J. C. SCOTT.

SIR,—We should like to comment on certain points in the report of the M.R.C. Working Party on Sterilisation (Feb. 28) and in your leading article on it.

Though the surgeon or doctor may be legally responsible for a patient under his care, he has a right to expect that materials handed to him purporting to be sterile shall indeed be so, particularly in a hospital. The point at issue is, who shall be responsible for the sterilisation of these materials?

The processes of heat sterilisation are primarily physical and engineering problems, and once the conditions of time and temperature have been accepted for general application, bacteriology hardly comes into it. But sterilisation, as a unit process involving diffusion, heat transfer, and plant operation, requires rather more than " rudimentary knowledge of bacteriology, physics, and chemistry ".

For many years the correct type of technological training has been incorporated in courses for degrees in pharmacy and for ıe Pharmaceutical Society's diploma, together with a sound background of bacteriology and physical chemistry. The bacteriological training is oriented to sterilisation processes, aseptic handling, and disinfection.

This leads us to the conclusion that a pharmacist, by training and outlook, is the most suitable person for undertaking, and being responsible for, the supply of sterile materials. Indeed, if his professional services are to be properly used, he should also be responsible for the training of personnel, and for formulating techniques and procedures for the different types of sterilisers installed in hospitals. His background knowledge of plant operation should enable him to appreciate the limitations and frailties of the accessory instruments used with sterilisers and to cooperate well with the engineer.

Alike in the report from the Nuffield Provincial Hospitals Trust, the report of the M.R.C. working party, and in your editorial, the pharmacist's claims and his training are ignored. Yet in at least two London hospitals there are plans for a central sterilising department to be placed in charge of the pharmacist.

On the technical side we expected the working party to provide authoritative and clear statements of principles to be observed and techniques to be followed. Instead, though most of the relevant principles are mentioned in the report, they are contradicted or confused by loose comments elsewhere. Furthermore a number of statements give a wrong conception of the physical and physicochemical phenomena on which sterilisation depends.

To us the most dangerous implication (p. 425), in spite of partial contradictions elsewhere, is that, whilst downward-displacement sterilisers can only be made to give satisfactory results if they are properly used by skilled operators (which is true), high-vacuum sterilisers will produce sterile products when they have been badly packed or overloaded, and their use would therefore offset the shortcomings of operators who do not understand the principles of the process. A person who is not trained to appreciate the problems associated with a downward-displacement steriliser will certainly not be in a position to judge when a high-vacuum steriliser is not functioning properly, and the results of such ignorance could be even more disastrous than the unfortunate experiences described by the Nuffield publication. A high-vacuum steriliser is a complex piece of plant, especially when it is fully automated; and, for the safety of patients, the operator should be able to detect defects as they occur so that immediate action may be taken. Adequate routine maintenance is essential; but it can be only a secondary safeguard, as it is designed to restore to proper functioning parts obviously defective. The discovery of a faulty non-return valve in a monthly check is small consolation to a surgeon with infected cases in his beds, especially if the steriliser operator then recalls that he could not obtain the stated degree of vacuum although he had pushed the right buttons.

It may be wishful thinking, in the middle of the second column on p. 426, to say " there will be little loss of water [from cotton or hydrophilic material] until a point is reached where the absolute pressure in the chamber equals the equilibrium vapour pressure over the material ". Evaporation takes place continuously as soon as the *partial pressure* of water vapour in the ambient atmosphere of the chamber is reduced in magnitude to the equilibrium water-vapour pressure (E.W.V.P.) associated with the material. As the chamber pressure is further reduced, the rate of evaporation from the material will increase until the absolute pressure equals that of the E.W.V.P., when ebullution will theoretically take place if the water is free. Unfortunately two other factors also become important. With cellulosic materials containing less than 6% water, most of this water is " bound ", and a high level of energy is required to allow it to break away and evaporate; and, secondly, in the practical case of a dressing, the latent heat for any evaporation must be obtained from the sensible heat of the material, and the temperature is thus reduced, creating a new set of conditions. Furthermore any water vapour which is

produced will diffuse *into* the residual air to form an intimate air/water vapour mixture and is unlikely to " sweep the residual air ahead of it ".

The mechanism of gaseous diffusion is also ignored at the bottom of the second column on p. 426. Air will not concentrate " as a bubble " but again will more likely form with any steam an intimate mixture which may have a near-steam density and is unlikely to be displaced subsequently by gravity.

In the first column of p. 426 there is a loose statement of " drawing two or three times a 50% vacuum with alternate admission of steam . . . on bottled fluids ". This is a procedure even a novice would never repeat, because of the memory of the resultant mess in the chamber!

The presence of pyrogens in any solution (p. 432) indicates weaknesses in preparative techniques *prior to* sterilisation and not of the sterilisation process. Sterilisation exposure times and pyrogen content cannot be correlated.

The report repeatedly draws attention to the adverse effects produced by running a chamber jacket hotter than the chamber. In fact, there seems enough evidence to show that the use of a jacket is of no benefit, and probably harms the materials to be sterilised. In our view a jacket is an expensive means of thermal insulation of the chamber.

We are not convinced that vacuum of the order mentioned in the report (5–20 mm. Hg abs.) can be adequately measured by the standard commercial instruments usually employed.

Since sterilisation is a highly skilled procedure, we believe that there is no substitute for constant supervision by fully trained personnel responsible to a technologist, such as a pharmacist, who has the necessary scientific background.

Lastly we would like to know what is meant by " imperfectly sterilised articles ".

E. SHOTTON
Professor of Pharmaceutics
D. TRAIN
Lecturer in Pharmaceutical Engineering Science.
School of Pharmacy, University of London, 29, Brunswick Square, W.C.1.

CHILD HEALTH AND CHILD PSYCHIATRY

SIR,—Dr. Mildred Creak's lecture, published in your last issue, states the problems comprehensively and lucidly. As one who has felt for years that only a marriage of pædiatrics with psychiatry will enable us to understand the child's private world, her lecture has given me great pleasure.

During ten years' experience with public-health clinics I became increasingly convinced that every child develops through a series of emotional crises. The wholly subjective, archaic, and savage bundle of emotions which is a young babe could not develop into the comparatively civilised 5-year-old unless the pressures and experiences became deeply embedded.

Years of psychiatric practice, on the other hand, have taught me humility. I have seen how painstaking is the effort, how slow and small the results. Perhaps this is just as well. If we had the power over others which we wish, our mistakes might be taken over wholesale.

Although we know the size of the problem, we also realise that sensitisation to, and acceptance of, the necessary new discipline will take much time. If we wish to develop the personality of the therapist, together with his understanding, field-work offers in my opinion the best chances.

To return to Dr. Creak's simile, if child psychiatry is the child of divorced parents, there is no reason why we should not woo this adolescent into a marriage with the more secure, eminently suitable partner of pædiatrics. This might be best done by joint practice in both fields. The points in favour of such effort are numerous. It would remove much suspicion; it would offer an easy, acceptable form of correction because the patient's need is considered, not the therapist's personality; and it would also make the best use of the limited number of people available for this type of work. Last, but not least, it would create the necessary precedent, out of which, as so often in the past, stable practice might grow.

London, S.W.15. HEDY SYMONDS.

IS PEPTIC ULCER AN ENDOCRINE DISEASE?

SIR,—With reference to my paper (Jan. 17) on Islet-Cell Tumour of the Pancreas Associated with Peptic Ulceration, your editorial, and subsequent letters, the following recent data may be of interest.

The patient remains very well and free from indigestion, and is gaining weight. Laboratory investigations: Hb 12·4 g. per 100 ml.; blood-urea 25 mg. per 100 ml.; sodium 143, potassium 4·5, chloride 105 mEq. per litre; plasma calcium 11, phosphorus 2·6 mg. per 100 ml.; serum acid phosphatase 1·1, alkaline phosphatase 11 units per 100 ml.; Sulkowitch test for urinary calcium normal. X-rays of abdomen, lungs, bones, and pelvis reveal no abnormality.

I am very grateful to my ex-colleague, Mr. W. MacBeth, for this information.

Chelmsford and Essex Hospital. B. W. T. PENDER.

ATHEROSCLEROSIS AND ISCHÆMIC HEART-DISEASE

SIR,—I have read with interest Dr. W. B. Robertson's article (Feb. 28) in which he reports on the low incidence of ischæmic heart-disease and the frequent occurrence of atherosclerosis in Jamaica. He compares his results with those of Tejada and Gore,[1] who studied the same problem in New Orleans and in Guatemala.

Contrary to Dr. Robertson's results, these workers find a parallelism between the incidence of atherosclerosis and ischæmic heart-disease. The divergent results of these investigations, in which the same method for estimating the degree of aortic atherosclerosis was used, raises the question whether postmortem examination alone can give a complete answer to the atherosclerosis problem. Postmortem examination, though important and indispensable for the detection of atherosclerotic lesions and the study of its complications, does not provide enough information on the incidence and severity of atherosclerosis in the population.

In a recent paper [2] I suggested that radiography of the abdominal aorta is a valuable additional aid for the investigation of these problems. Although this method is limited to the detection of advanced atherosclerosis, it has the great advantage of studying the incidence of calcified atheroma in a large number of unselected cases during life. I believe this procedure merits more attention in clinical surveys connected with arteriosclerosis. I examined radiographs of the abdominal aorta in many elderly individuals, who attended the orthopædic or physiotherapy outpatient departments for minor ailments, and who had no clinical indication of coronary heart-disease. In my paper I pointed out that a high percentage of these patients, particularly women, show evidence of extensive aortic calcification often involving the whole length of the aorta. I therefore arrived at the same conclusion as Dr. Robertson—that there is no close correlation between calcified atherosclerosis and the incidence of ischæmic heart-disease. This finding is no contradiction to the widely held view that some degree of atherosclerosis of the coronary arteries plays a part in thrombus formation. But my observation suggests that extensive calcified atherosclerosis is to some extent a protective process against thrombus formation.

Dr. Robertson does not give any information regarding the frequency distribution of atherosclerosis between the two sexes, which I believe to be an important feature in these surveys

1. Tejada, C., Gore, I. *Amer. J. Path.* 1957, **33**, 887.
2. Elkeles, A. *Lancet*, 1957, ii, 714.

because it may provide a clue to the ætiology of atherosclerosis. I found a greater prevalence of aortic calcification in females after the age of 60, and Epstein [3] made similar observations in the U.S.A. He refers to Hasse [4] and Rokitansky,[5] who over a century ago knew of the greater prevalence of aortic atheroma in women.

I fully agree with Dr. Robertson that extensive calcified atherosclerosis is compatible with health and a long life, and I may add that the prevalence of calcified atherosclerosis in women could perhaps explain why they live longer than men.

London, W.1. A. ELKELES.

FLATS FOR INDIGENT DOCTORS

SIR,—I should be grateful if you would afford me the hospitality of your columns to bring to the notice of the medical profession a new venture of the Royal Medical Benevolent Fund.

Owing to the generosity of the late Mr. J. T. M. Giffen, F.R.C.S., a house has been purchased in an attractive residential area off Putney Hill. It has been converted into five self-contained flats and has a large and pleasant garden. Each flat consists of sitting-room, bedroom, kitchen, bathroom, and lavatory, and the rooms are by no means small.

These flats are rent-free and are intended for retired doctors and their wives in reduced circumstances. A maintenance charge of £25 per annum is to be made and residents will supply their own heating and lighting. The conversion of the house into flats is almost complete.

The committee will now be glad to receive inquiries from any members of the medical profession who might consider applying for one of these flats. Fuller information will be given by the Secretary, Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, to whom all communications should be addressed.

R. M. HANDFIELD-JONES
Chairman, Committee of Management.

PHENYLBUTAZONE AND PROLAPSED INTERVERTEBRAL DISCS

SIR,—I was interested to read Dr. Gillhespy's letter of March 7 and to see his results. I feel it a pity that he did not let us know whether the protrusions were annular or part of the nucleus pulposus, as these react differently to different forms of treatment. He mentions that some of the cases had neurological signs. Were any of these included in the 83% improved in four days or were they all in the 17% of failures?

He makes three staggering statements (the italics are mine):

1. "It has been proved that the nucleus pulposus erupts through a tear in the annulus fibrosus under the posterior longitudinal ligament in *all* disc lesions." Does he really believe that the annulus never protrudes to cause symptoms?

2. "The prolapsed portion can return spontaneously, and this accounts for sudden improvements *despite* therapy." Surely the thousands of patients who are relieved of their pain immediately by manipulation—and I emphasise "immediately"—cannot have been treated at the precise moment when spontaneous recovery was taking place.

3. "Herniation of the nucleus pulposus can occur *only* in hyperextension or overloading of the vertebral column." One has only to listen to the patients' description of the onset of pain to learn that in most cases flexion has caused the attack to start, and frequently with no overloading.

3. Epstein, F. H. *ibid.* p. 1232.
4. Hasse, K. Krankheiten cer Zirkulations-und Respirationsorgane. Leipzig, 1841.
5. Rokitansky, C. Handbuch der pathologischen Anatomie: Handbuch der speziellen pathologischen Anatomie; vol. 2, p. 544. Vienna, 1844.

I have been using 'Butazolidine' in specially selected cases with considerable success. These cases have pain either in the lower back or a leg or both, due to a protrusion of part of the nucleus pulposus. Spinal traction is given with improvement at first; when the improvement ceases despite further traction, butazolidine is given instead in small doses—200 mg. b.d. for 14 days. The majority of patients are rid of their pain within a few days, and many have no further pain after stopping the tablets. I hope to write up the results at a later date.

London, W.1. R. BARBOR.

SOFT DRINKS

SIR,—"Secret" drinks are the soft drinks most needing new legislation, but these are totally ignored in the recent recommendations of the Food Standards Committee.[1] As an example, "cola" drinks are drunk in large amounts by children and adolescents. Some of their ingredients are secret and are imported from the U.S.A. Though parents ask doctors if such drinks are safe, no answer is possible. Neither the Ministry of Health nor the importers can tell doctors their composition.

Surely any new legislation should make it impossible for any "secret" drink to be sold, especially as many people believe that some "secret" soft drinks contain stimulating drugs of addiction.

London, W.1. FRANKLIN BICKNELL.

FATAL TUBERCULOSIS IN A GENERAL HOSPITAL

SIR,—I am surprised there has been no previous comment on the article by Dr. Treip and Dr. Meyers (Jan. 24) dealing with patients dying from tuberculosis in a general hospital, in many of whom the disease had not been diagnosed during life. The article is very interesting not only for what is said, but also for what is not said. In the discussion appears the sentence: "The problem of these patients is one of prevention and hence of case-finding outside the hospitals." I seek in vain, however, for any indication in the article that those in the hospital took any steps to encourage this case-finding, which is so manifestly desirable; and indeed one might well ask what should be done in such cases, which are common enough elsewhere.

The article reports that during the decade 1948–1957 there were 128 "tuberculosis necropsies" and from fig. 2 one can take it that tuberculosis was not diagnosed (although sometimes suspected) until after death in 31 of these cases. These latter must have been treated in various wards or departments other than those accustomed to the precautions needed in managing open tuberculosis (e.g., case 4 with large-bowel obstruction and extensive bronchopneumonia; case 2 fibrosarcoma of breasts with extensive lung lesions), and the potential risk to hospital staff is evident. No doubt this risk has not been overlooked; but what about the homes from which these patients came? Cases 3, 4, 10, and 11 were all old people whose histories make it only too likely that they had been coughing up infectious sputum for weeks or months: were the respective medical officers of health informed of the post-mortem results so that preventive work and contact examination might, although delayed, be put in hand? Indeed in any given hospital (whether teaching or other) who should regard it as his job to pass on such important information? The diagnosis having been made at the postmortem examination it is too late for formal notification that the patient is suffering from the disease. The pathologist might with some reason disclaim responsibility for taking any action once he has reported to the clinical side.

1. See *Lancet*, March 7, 1959, p. 515.

Has one to hope that the particulars will be included in the hospitals' report to the family doctor, and, if he is prevention-minded, be sent on to the medical officer of health? I do not know the answer, nor what should be done in the odd case where a patient is found dead and active tuberculosis is discovered at the postmortem examination ordered by the coroner. I hope someone can make constructive suggestions.

East Sussex County Council, Lewes. F. LANGFORD
County Medical Officer of Health.

PRIMARY MICRO-ORCHIDISM

SIR,—Dr. Ferguson-Smith's paper (Jan. 31) is of great scientific interest and has many important implications for those studying the problems of genetical and apparent sex.

The author describes the results of testicular biopsies carried out on mentally deficient children, and he expresses the hope that it will be possible to do something to prevent or modify eventual sterility, gynæcomastia, and eunuchoidism in these children. One must agree with this hope.

It seems relevant to ask the following questions, the answers to which do not appear from the text:

1. Were the children's parents fully informed of what was being done and the reason for it?
2. Were the testicular biopsies carried out under general anæsthetic?
3. Was the author satisfied that, for example, case 6, with a chronological age of 11 years 4 months and a mental age of 8 years 9 months, was not likely to suffer the psychological damage that might be expected from an operation of this kind?
4. If the parents of these children did, in fact, volunteer on their behalf, and if one of the children had died from the anæsthetic or some other mischance, how would the facts have been reported to the coroner?

Of course if the investigation was carried out entirely in the expectation of devising some treatment for the children, and it was merely hoped that some interesting information might be obtained by the way, then none of these questions needs to be asked. The first paragraph of the discussion, beginning "The main purpose here is to demonstrate that a defect already exists . . ." would, however, seem to indicate that such is not the case.

London, N.1. R. E. W. FISHER.

*** Dr. Fisher's letter has been shown to Dr. Ferguson-Smith, whose reply follows.—ED. L.

SIR,—I am glad of the opportunity of replying to Dr. Fisher's letter, and also of taking up a matter which it had not seemed appropriate to discuss in detail in the paper.

The decision to do biopsies of these cases was taken after most anxious thought, and consultation with Mr. W. S. Mack, who actually did the biopsies, and others closely concerned including Dr. Bernard Lennox. Mr. Mack has had very great experience in the handling of cases of sterility and hypogonadism of all sorts and believes that testicular biopsy is of enormous value both in increasing the general understanding of the problem and in handling the individual patient. These two aspects often cannot be separated. While it was discovered that there was no prospect of rendering these patients fertile, and this presumably also applies to those cases with normal intelligence, there remains a real prospect of diminishing the disabilities of eunuchoidism at puberty, and it is only possible to plan treatment if we know exactly what is happening. Such knowledge is of advantage for the individual patient.

So far as the individual questions are concerned:

1. The parents were fully informed of the nature of the biopsy procedure and the reason for it as stated here, though, of course, the question of sex reversal was not mentioned. Mr. Mack wrote personally to the parents explaining the position.
2. Yes.
3. This is a matter for the clinician concerned. Mr. Mack is perfectly happy about this.
4. The position here is exactly the same as in the case of any death under a minor diagnostic procedure—for instance, from lumbar puncture or catheterisation.

With regard to Dr. Fisher's last sentence, "the main purpose" was of course the purpose of the discussion, not that of the investigation as originally planned.

M. A. FERGUSON-SMITH.

CHILDREN IN HOSPITAL

SIR,—In his reply last week to Sir Harry Platt's letter (Feb. 28) which disavowed the suggestion that the Committee on the Welfare of Children in Hospital "wished to see . . . the breaking up of children's hospitals" Dr. David Lawson recants and apologises. But he then proceeds to direct the accusation at me, and in support writes:

"Lord Cohen stated categorically in the House of Lords (*Hansard*, House of Lords, Feb. 12, 1959, col. 185) that to *break up Queen Mary's and to distribute the acute cases around adult hospitals* would 'conform to the desiderata of the Welfare of Children in Hospital Committee's Report'."

Dr. Lawson should not allow his passionate advocacy to distort the truth. *Hansard* reports me in col. 204 as saying that "nearly 80% of the children now in Queen Mary's stay for less than a month, which means that they *could be dealt with satisfactorily in acute general hospitals with adequately equipped children's units*, and so conform to the desiderata of the Welfare of Children in Hospital Committee's Report". I then pleaded for a review (on a basis which Lord Crook found "so impeccable that I could accept it wholeheartedly") of a situation which allowed hundreds of beds to remain empty when there is a compelling and urgent need for hospital accommodation in many fields. I then proceeded: "It may very well be that as a result of that review some hospitals which are now children's hospitals will, and should, be retained solely for the purpose of treating children" (col. 205).

I trust that Dr. Lawson will once again "hasten to withdraw and apologise".

The University, Liverpool, 3. COHEN OF BIRKENHEAD.

SIR,—As members of the senior medical staff of Queen Mary's Hospital for Children, we wish to express our appreciation of the space which you have allotted to this subject, particularly in relation to the proposed closure of our hospital.

There is one important aspect of our present problem which has received little attention. The negotiations about the ultimate fate of the hospital have been going on for about nine months. During this time the hospital has been and still is very busy with its customary inpatient and outpatient work: at the time of writing there are 407 children in the hospital, of whom 185 are short-stay and 222 long-stay. Whatever may be said about the problem of empty beds, the day-to-day problems of dealing with the children in the occupied beds are surely matters of prime concern, giving rise to matters of maintenance,

staffing, and administration which simply cannot be shelved without detriment to the ordinary working of the hospital and, indirectly, the welfare of its patients. Yet it is our experience now that almost every problem, large or small, is being shelved on the grounds that the fate of the hospital must first be decided. We have reason to believe that the level of clinical care within the hospital has not deteriorated during this trying period; but we are conscious of unfilled vacancies in establishment and other difficulties which impose severe handicaps on our efficiency as a clinical team and which must, if protracted, affect morale and welfare of patients and staff.

The administrative problem posed here and elsewhere (notably in fever and orthopædic hospitals, and in sanatoria) by empty beds is admittedly serious, and we have endeavoured now, as in the past, to take a realistic attitude towards the desirability of utilising to best advantage our own empty beds (about 200 in number) and building ground. At the same time, we have cooperated with the regional board and other authorities in building up our general pædiatric services, including the provision since 1954 at considerable public expense of additional thoroughly modern cubicles (48 in number), sterilising-rooms, kitchens, school, and pathology and radiology departments, and the creation of new senior posts in medical and surgical pædiatrics, radiology, pathology, orthodontics, ophthalmology, and so forth, with corresponding appointments in junior medical, nursing, and ancillary staff. If long-term planning is the key to the present situation—and we do not dispute the need or the opportunity for this—then we may presumably be pardoned for assuming that, in our case, the plan has been the successful, very recent, conversion of a long-stay into a general children's hospital, with comprehensive educational and other facilities.

We have no option but to await hopefully the decision of the central planners; but it is surely of great importance that decisions of this kind should be based upon a realistic assessment of the functions and value of the hospital in question rather than on unrelated financial and administrative expediencies.

H. M. T. COLES
L. G. KINGDOM
C. W. KESSON
MARGARET MANFORD
R. H. METCALFE
H. H. NIXON
P. K. ORTON
E. D. L. SIMPSON
G. T. STEWART
R. G. THOMAS
B. C. H. WARD.

Queen Mary's Hospital for Children, Carshalton.

NEW-TYPE OXYGEN CYLINDERS: A WARNING

SIR,—I read with interest Dr. Marcus Bird's letter (Jan. 31). I have found the 'Universal Handwheel' key quite unsatisfactory and pointed out over twelve months ago to the British Oxygen Company's representative the following disadvantages:

1. Occasionally it is quite impossible, except by the greatest exertion, to turn on the cylinder with the key supplied, as the gripping power is limited in comparison with the old-fashioned spanner.

2. One must keep a special spanner to tighten the hexagonal nut on the cylinder.

The majority of anæsthetists I have spoken to dislike this universal handwheel key, but I am assured by the British Oxygen Company that it was by popular demand on the part of anæsthetists that they were produced. The British Oxygen Company's representative has promised me he will take the matter up with headquarters.

I wonder what would have happened if the patient Dr. Bird refers to had been on controlled respiration, when the situation might have become desperate owing to the fact that the latest equipment supplied had failed to do the job it was intended to do.

Little Bromwich General Hospital, Birmingham. EUGENE THOMAS.

NEONATAL HYPERBILIRUBINÆMIA

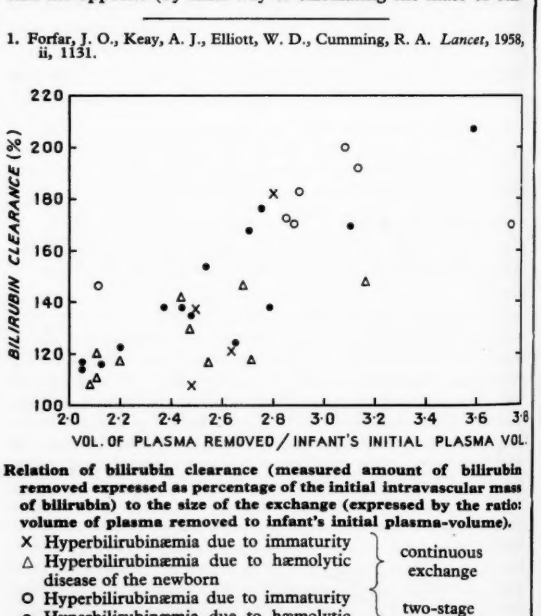
SIR,—May I use your space again in order to reply to Dr. Forfar and his colleagues (Feb. 7)?

I used the term "biological experiment" as opposed to experiments in physics or chemistry. They can both be scientific, but with biological experiments all the variable and uncontrollable factors mentioned by Dr. Forfar and his colleagues have to be taken into consideration when analysing the results, and moreover statistical averages have a limited value.

For instance, I fail to find any meaning in the fact that in the 4 exchange transfusions (8b, 15b, 6b, 21) of less than 50 ml. per lb. the average minimum mass of bilirubin removed (granting for the moment that this figure has a real, separate existence) was 8·1 mg.; but I shall be very interested to know why in 2 of these cases (8b, 15b) the estimated minimum mass of bilirubin removed is less than the drop in the circulating mass of bilirubin produced by the exchange, while in case 21 the minimum mass of bilirubin removed is five times greater than the drop in the circulating bilirubin (see table I of their article [1]).

As Dr. Forfar and his coworkers in their long reply do not mention my criticism that their results are based on a logical fallacy I take it that this was the part of my letter which they found "incomprehensible". I shall try again to make this point clear. In their paper they say: "The effectiveness of exchange transfusion cannot be judged by the fall in serum-bilirubin . . ."; and yet this is exactly what Dr. Forfar and his coworkers have done, only reversing the argument. Instead of saying that a larger drop means higher efficiency they maintain the opposite (by their way of calculating the mass of bili-

1. Forfar, J. O., Keay, A. J., Elliott, W. D., Cumming, R. A. *Lancet*, 1958, ii, 1131.



Relation of bilirubin clearance (measured amount of bilirubin removed expressed as percentage of the initial intravascular mass of bilirubin) to the size of the exchange (expressed by the ratio: volume of plasma removed to infant's initial plasma-volume).

× Hyperbilirubinæmia due to immaturity
△ Hyperbilirubinæmia due to hæmolytic disease of the newborn
} continuous exchange

○ Hyperbilirubinæmia due to immaturity
● Hyperbilirubinæmia due to hæmolytic disease of the newborn
} two-stage exchange

rubin removed) without offering any proof for this. When using in their calculations the figures of minimum mass of bilirubin removed, Dr. Forfar and his colleagues obviously forgot how these figures were derived. They gave them a separate existence, while they are nothing else but a confusing way of relating the volume exchanged with the level of bilirubin at the end of the exchange. These figures cannot be used as a "comparative index" unless one has proved first that the relationship of those figures to the amounts of bilirubin actually removed is not influenced by the rate and volume exchanged—the two main variables studied by Dr. Forfar and his coworkers.

As this basic mistake is enough to invalidate all the results presented by Dr. Forfar and his coworkers I shall not discuss again their other omissions although their reply on these points is full of irrelevant and dogmatic statements.

Dr. Forfar and his colleagues complain that I have not said how the adjustment, as far as the initial serum-bilirubin level and weight of the baby, should be done. The accompanying figure shows the number of the cases studied and the principles followed in the analysis of the results.

Athens. TIMOS VALAES.

A STATISTICAL DIFFICULTY

SIR,—Before launching into any explanation of my statistical difficulty (Feb. 28, p. 435), I should have looked into my "Bradford Hill". I might have guessed that my learned friend would have included that item in "problems and difficulties" in his *Principles*. He has shown the matter very clearly in a set of fictitious figures for districts with populations of different age-structure. I regret my oversight—for I should have acknowledged Professor Hill's exposition.

London, S.W.1. A. R. SOUTHWOOD.

VENTRICULAR STIMULATION BY CATHETER ELECTRODE

SIR,—The treatment of ventricular standstill by an external electric stimulator has become well established since its description by Zoll.[1] A stimulator designed by one of us (J. G. D.) has been in use in this hospital since 1956, and its use in two cases was reported by Leatham et al.[2]

Effective stimulation of the ventricles with external chest electrodes requires 40–200 volts and may result in considerable distress from painful contractions of the pectoral muscles. Since stimulation may need to be continued for a long period this is a serious disadvantage. It can be overcome by implanting an electrode in the myocardium as is widely practised in centres using pump oxygenators for repair of ventricular septal defects, and has been reported from Guy's Hospital by Dr. Clark and his colleagues (Feb. 21). An alternative, which is applicable to medical patients with heart-block requiring treatment, is to use a catheter electrode in the right atrium as suggested by Hopps and Bigelow.[3]

A man, aged 68, had had occasional Stokes-Adams attacks for five years and was admitted to St. George's Hospital in October, 1958, with an increase in frequency of the attacks to several each day. His pulse was regular at a rate of 20 per minute, and an electrocardiogram showed 6 : 1 atrioventricular block.

He was treated with ephedrine and isoprenaline without any increase in the ventricular rate. Four days after admission he had a lengthy Stokes-Adams attack. A nurse applied the chest electrodes of the external stimulator, and stimulation was started at a rate of 60 per minute, using 160 volts. Although two to three minutes had elapsed since ventricular standstill, good femoral pulses followed each stimulus, and after half an hour the patient began to recover consciousness. He soon became considerably distressed by the stimulation. Any reduction in voltage or cessation of stimulation resulted in ventricular standstill. It was therefore decided to use an electrode in the right atrium. A no 5 Cournand catheter bearing an electrode just proximal to the tip, was advanced to the right atrium via an antecubital vein and the position checked by a chest X-ray One terminal of the stimulator was attached to the catheter electrode and the other remained on a chest electrode Effective ventricular stimulation could then be obtained with approximately 20 volts. This caused only a slight twitch of the pectoral muscles and did not distress the patient at all. He was able to converse with his wife at this time. Over the next nine hours there were five episodes of failure to react to the stimulator, each responding to a temporary increase in the voltage. Finally ventricular standstill occurred and failed to respond to any stimulus up to about 100 volts.

Postmortem examination showed no evidence of any damage to the right atrium. Histological examination of the heart, for which we are indebted to Dr. D. Dexter, showed disappearance of Purkinje cells and diffuse endocardial fibrosis at the site of the left bundle of His. There were a few small areas of necrosis in the muscle of the left ventricle, but there was only moderate coronary atheroma and no infarction.

Stimulation of the ventricles using an electrode catheter in the right atrium was successfully carried out for several hours in this patient and did not give rise to the severe discomfort which accompanied external stimulation. The final failure to respond may have been due to myocardial anoxia resulting from the episodes of standstill following a long period at a very slow ventricular rate.

The electrode catheter has been introduced in two other patients with Stokes-Adams attacks. In one it remained in position for three days and was used to stimulate during a period of slow ventricular rate, and appeared to be effective. In the other patient, who was having frequent attacks of ventricular standstill, it was placed in the right atrium during cholecystectomy in case stimulation should be required, but this proved unnecessary. There appears to be no reason why an electrode catheter should not remain in position for a long period if required, but it would probably be wise to heparinise the patient in order to minimise the risk of venous thrombosis.

While there is no doubt about the value of an external stimulator as a temporary measure in cardiac surgery, its usefulness may be questioned in patients with heart-block due to disease of the conducting system. Survival for up to two years following treatment has, however, been reported by Zoll [1] and Zoll et al.[4] It is also encouraging to find that the disease is often limited to the conducting system, and generalised coronary-artery or myocardial disease is mild or absent. The use of a stimulator to tide the patient over a period of severe attacks, or to provide an interval for drug therapy to be instituted, would seem to hold some hope of a useful prolongation of life in such cases. The implantation of a wire electrode in the myocardium might even be considered (W. P. Cleland, personal communication).

There are no serious problems in the design and construction of an external electric stimulator, but there is debate about the most effective wave-form for the stimulus. Zoll used a monophasic square wave with a duration of 2–3 milliseconds, while Hopps and Bigelow employed a thyratron oscillator circuit producing a sharply peaked pulse with exponential decay, the duration

1. Zoll, P. M. *New Engl. J. Med.* 1952, **247**, 768.
2. Leatham, A., Cook, P., Davies, J. G. *Lancet*, 1956, ii, 1185.
3. Hopps, J. A., Bigelow, W. G. *Surgery*, 1954, **36**, 833.
4. Zoll, P. M., Linenthal, A. J., Norman, L. R. *Circulation*, 1954, **9**, 482.

being 3–4 milliseconds. A similar wave can be produced by discharge of a condenser, and such an instrument is cheap and simple to make.[2] It has proved effective in our experience of eight cases, and has been employed successfully using low voltage with direct myocardial electrodes by the thoracic surgical department at Hammersmith Hospital.

One of us (B. F. R.) is in receipt of a research grant from the board of governors, St. George's Hospital.

J. G. DAVIES
A. LEATHAM
St. George's Hospital, London, S.W.1. B. F. ROBINSON.

ASSOCIATIONS WITH COMMERCE

SIR,—Much public interest has now developed around the great sociomedical problems of obesity, carcinoma of the lung, bronchitis, and myocardial infarction. The burden of these on our society increases each year. Many differing ætiological factors are put forward and much controversy centres on preventive measures. Great vested interests are at stake.

Might a plea be put that those writing and talking on these subjects should state not only the position they hold in hospital or university, but also any paid advisory functions they exercise on behalf of large companies?

Very few in our profession and practically none of the general public realise that some holders of professorial chairs and other important positions in the medical world also act as expert advisers to industrial concerns. This may not affect their judgment, but they may reasonably be asked to "declare their interest".

Central Middlesex Hospital, London, N.W.10. HORACE JOULES.

Medicine and the Law

Parental Consent

FAILURE by parents to provide necessary medical care and attention for their children is an offence punishable by fine or imprisonment [1]; and, if a child dies in consequence, the parents may be charged with manslaughter.[2] Among the most tragic of such cases are those which arise from the refusal of the parents, on grounds of conscience, to permit an operation. In such cases, even the possibility of a manslaughter charge may not induce the parents to give their consent; and to punish the parents afterwards will not restore the child to life. Two recent Canadian cases point to a possible solution.

The first concerned a 14-year-old Manitoba boy who was accidentally shot.[3] His father refused permission for a blood-transfusion. The hospital, considering that nothing could be done, made no approach to the Manitoba Government. Some days later the Manitoba Government heard of the matter and the Attorney-General asked the juvenile court for custody of the boy. The Attorney-General was apparently relying on a provision in the Child Welfare Act which made it an offence for parents to fail to provide medical care. The Act provides that 14 days should elapse "where possible" between the first action and the hearing. In this case the hearing was called four hours after the initial action, but lawyers representing the parents were successful in obtaining a one-day adjournment. During that day the boy died. At the inquest a doctor testified that, if the transfusion had been given, the boy at worst would have lost a leg. The jury recommended changes in the Child Welfare Act.

In the second case the parents of a baby girl refused permission for a blood-transfusion which might save her life.[3] The Attorney-General for Ontario secured a court sitting in a Toronto hospital; the court made the girl a ward of the Children's Aid Society, which in turn gave permission for the transfusion. It was later announced that the Children's Aid Society would ask the Ontario Government for legislation to allow doctors to give blood-transfusions in an emergency without parental consent or court authorisation.[4]

If similar circumstances arise again in England, it would seem that the child could be brought before a juvenile court under section 62 of the Children's and Young Persons Act, 1933, as being in need of care and attention. The court could then commit the child to the care of "a fit person" including for this purpose the local authority. In many respects the local authority would be a suitable body to assume parental rights, but their procedure might be too slow in an emergency. On the other hand, the Canadian proposal that doctors should have power to act in an emergency without the authority either of the parents or of a court raises far-reaching issues of public policy.

1. Children and Young Persons Act, 1933.
2. *Lancet*, 1958, i, 583.
3. *Times*, Dec. 15, 1958. *Globe and Mail*, overseas edition, Dec. 24, 1958.
4. *ibid.* Dec. 20, 1958.

Parliament

Work for Older People

IN the House of Commons on March 6 Colonel RICHARD GLYN drew attention to the rising average age of the population and the consequent importance of making full use of the working capacity of older men and women and asked the Government to promote further research into the problems of their employment. It was estimated, Colonel Glyn continued, that in twenty-five years for every 100 people of working age there would be 30 people of pensionable age. If they all retired at the earliest possible moment, the burden on those of working age would soon become oppressive. Older people should therefore be encouraged and helped to continue working. Mr. Le Gros Clark in his studies for the Nuffield Foundation had come to the conclusion that some 20% of elderly people could not continue in their accustomed jobs, but would need alternative work or modified conditions. Colonel Glyn did not wish to minimise the difficulties of placing elderly employees and he would like to see further research of this kind. It was important in his view that the results of such research should be published in an easily understandable form so that the elderly worker, the employer, and the younger worker should all understand the need for the postponement of retirement.

Mrs. EVELYN EMMET said that when she considered the steady growth of the social services to help old people, she was struck by the absence of the main factor that made for happiness and good health among the aged—the feeling that they were useful and appreciated by the community. The acute loneliness of old people and the feeling of having outlived any useful purpose was a tragedy and a reproach to our civilisation. Turning to the special problems of middle-aged and elderly women, she asked that in future every girl should receive a training for work of some kind, which would enable her when she had finished with parenthood to return as a useful full-time or part-time worker. Mrs. Emmet was sure that at present we were losing the opportunity of the benefit of extremely valuable people. More nurses, midwives, and teachers would come back if they were encouraged and helped and the job was suited to them as well as them being suited to the job. If old age was to be protracted, we must make the best of it, and as a small country we could not afford to allow 8 or 9 million of our population to waste away as elderly people.

Mr. J. A. LEAVEY said that we shyed away from the idea of raising the retirement age, yet it was an unsatisfactory yardstick. Sir KEITH JOSEPH suggested that the Government should consider the argument in favour of having a fixed age for

receiving a pension (perhaps slightly higher than the present retirement ages of 65 and 60) without retirement conditions or the possibility of early pension increment. This would leave people free gradually to lessen their work—to choose, as Professor Cairncross had put it, " not whether to retire, but how much to retire ". We were moving towards an affluent society which would have more employment opportunities, simultaneously with more opportunities for education and leisure. We should ensure that our pension rules did not distort incentives as they did at present.

Mr. DOUGLAS HOUGHTON thought that the country must soon redefine its retirement policy. What did we expect to be a normal span of working life? Were we ready to lift the retirement age? Were we prepared to contemplate different retirement ages for different types of work? Should we continue to have an earlier retirement age for women? We must look at the standard working life anew and be prepared to accept something longer. All our thinking was governed by the retirement ages written into the present social security scheme.

Mr. RICHARD WOOD, parliamentary secretary to the Ministry of Labour and National Service, said that it was difficult to forecast the future numbers and composition of the working population, but, apart from economic changes, the population prospects suggested that there would be a material increase in the numbers of men and women over 55 at work and a decline in the number in the 35–54 age-group. He agreed that research on employment of the elderly was important. Some industries, particularly the woollen and allied textiles industry in the north of England, had sponsored research on their own account. The Department of Scientific and Industrial Research had been carrying out investigations into the effects of automation on skill and social organisation, and has been considering the difficulties which older workers find when they have to retrain at a fairly advanced age. Both in the laboratory and in the field the Medical Research Council had been trying to establish the effect of changes in jobs on middle-aged workers, and had undertaken a survey of manufacturing industries on Merseyside.

Mr. Wood accepted the need for further research and greater contact between research-workers and industry. He had decided that the best means would be to have a regular meeting of an interdepartmental committee representing the departments interested in this work. He believed that the best means of providing a link between the research departments and industry would not be to enlarge the committee, but, from time to time, to call one-day or two-day conferences to discuss the whole range of problems about which industry would give its view and the research-workers would tell industry how research in that line would be possible.

QUESTION TIME

Addiction and Responsibility

Sir FRANK MEDLICOTT asked the Minister of Health (1) if his attention had been drawn to a recent case in which an anæsthetist involved in a fatal operation admitted at his trial that he had been addicted for seven years to inhaling anæsthetic drugs, and if he would hold an inquiry into the circumstances under which such a tendency could have been unnoticed by the hospital staffs with whom the anæsthetist had been working over this long period; and (2) if his attention had been drawn to the practice of some anæsthetists of testing anæsthetic gases by inhalation; and what inquiries he proposed to make into the extent of this practice and its effects on the capacity of anæsthetists to perform their professional duties.—Mr. DEREK WALKER-SMITH, the Minister of Health, replied: I have studied with concern the proceedings in the case and am making further inquiries. I understand that many anæsthetists inhale small quantities of anæsthetic gases before administering them, and that they consider this a desirable precaution in the interests of their patients. I have asked the Committee on Drugs of Addiction, under the chairmanship of Sir Russell Brain, to consider whether any special measures are required in the light of this case.

Sir FRANK MEDLICOTT: Is the Minister aware that there is a feeling in some quarters that medical people are reluctant to testify against each other in matters of error or negligence and that the careful inquiries which he is instigating will possibly afford some reassurance on this very grave matter?—Mr. WALKER-SMITH: I am making inquiries to seek information about the reports said to have been made in the case. In the light of that information, I shall consider the general position further.

Dr. EDITH SUMMERSKILL: Will the Minister take into account that in the hospital where this tragic case occurred there was no medical administrator, and that although there was a medical committee with a chairman none of the consultants on this committee was prepared to condemn one of his colleagues? Here is an example of the necessity to follow the Bradbeer recommendation, to the effect that a medical administrator, who should have overall authority to take action in a case such as this, should be in charge.—Mr. WALKER-SMITH: That is one consideration to be borne in mind, although the matter goes a good deal wider than the point under reference. The question about transmission of information raises points of medical ethics which I may wish to discuss further with the profession.

Mr. HERBERT MORRISON: As it would appear from the proceedings of the trial that it was known by some of his medical colleagues that this doctor was addicted to this kind of thing, will the Minister ascertain why that was not conveyed, if it was not conveyed, to the hospital board, and if it was conveyed why the hospital board did not take action about it?—Mr. WALKER-SMITH: I am going further into the question about the extent of the knowledge which was referred to at the trial, although, as I say, on the general position it may be that certain questions of medical ethics arise which require further discussion with the profession.

Reinstatement after Wrongful Dismissal

Earl WINTERTON asked whether the Government would introduce regulations or, if necessary, legislation to ensure that where a court has held that a consultant or senior hospital medical officer in the National Health Service has been wrongfully dismissed by a hospital board he should be immediately reinstated in his original post.—The Earl of ONSLOW replied: Under the National Health Service Act, 1946, a statutory responsibility rests on hospital boards for the provision of specialist services in the hospitals under their control, and section 14 (2) of that Act specifically reserves to the boards the power to appoint consultants and similar staff. In addition, the terms and conditions of service of hospital medical and dental staff provide that a consultant or senior hospital medical officer who considers that his appointment is being unfairly terminated has the right of submitting his case to the Minister of Health before a decision to terminate the employment can be carried into effect. If in spite of these safeguards a consultant or other officer considers he has been wrongfully dismissed, his remedy lies with the courts, which may award damages. In those circumstances Her Majesty's Government are not satisfied that it would be justifiable to introduce regulations or legislation for the purpose the noble Earl suggests.

Earl WINTERTON: May I ask my noble friend whether he is aware that what I am asking him to do is to deal with the situation which has arisen in a case,[1] in which a distinguished consultant was held by one of Her Majesty's courts to have been wrongfully dismissed, and was awarded damages; and the Judge made some wounding observations, not only about the particular hospital board, but about the Ministry of Health? Will he give further consideration to this matter in order to avoid the possibility of a similar case arising in future?—The Earl of ONSLOW: I am fully aware of the case. It is almost impossible that it could happen again, because the contracts now are all the same, which they were not then, as this was a takeover case from the voluntary hospitals to the National Health

1. See *Lancet*, 1957, ii, 1342.

Service. But what I can tell your Lordships, which I think is of great value, is that the possibility is now being considered of amending the regulations to enable boards, where the appointments of consultants are terminated, through no fault of their own, but owing to redundancy, to put these doctors into other jobs without their having to go through the paraphernalia of answering advertisements.

Viscount ALEXANDER OF HILLSBOROUGH: I should really like to know, in view of the decision of the court, what steps the Ministry have taken to see that this particular professional man is properly rehabilitated. Has he been so rehabilitated? Has he been reappointed? Has he suffered no loss of status in his reappointment? What is the position?—The Earl of ONSLOW: I understand that he has a large private practice. He is also employed by a local authority. After the judgment the Minister wrote to the hospital board and said that he felt there was a moral obligation, and that should this man apply in the ordinary way for any work that was going, if he was as good as any other applicant that moral obligation should weigh in his favour.

Lord BALFOUR OF INCHRYE: Has this doctor received his damages; and is the Minister now prepared to reconsider retrospectively the case of this doctor who, according to the court judgment, has been wrongfully dismissed?—The Earl of ONSLOW: I understand that this doctor has received substantial tax-free damages, as awarded by the Judge, who at the time said that there was no possibility of reinstatement. After all, one has to remember that he was in a post which the hospital chose to divide into two separate posts. Do your Lordships really consider that it would be sensible, after five years, to tip out two perfectly good men, who were doing the work admirably, and to put him in, when the Judge himself, in this purely technical case, awarded him some £7000 damages and he is earning a good living in his own profession?

Government Food Laboratories

RESPONSIBILITY for the Low Temperature Research Station (at Cambridge), the Ditton Laboratory (at Larkfield, Kent), and the Pest Infestation Laboratory (at Slough) will be transferred on July 1 from the Council for Scientific and Industrial Research to the Agricultural Research Council. The two Councils consider that it is in the interests of the work for all Government research on food, other than fish, to come under one authority.

Appointments

EARL, C. J., M.D. Lond., M.R.C.P.: part-time consultant physician, Moorfields Eye Hospital, London.
LEE, R. E., B.M. Oxon., F.F.A. R.C.S., D.A.: part-time consultant anæsthetist, United Birmingham Hospitals.
MCNAUGHT, WILLIAM, M.D. Glasg.: consultant clinical pathologist, Scottish Borders hospitals group.
RYAN, R. P., M.B. Durh.: assistant M.O., Bristol.
TROUP, DOROTHY I., M.B. Edin., D.OBST.: school M.O. and assistant M.O.H., Coventry.
WYLIE, W. D., M.B. Cantab., M.R.C.P., F.F.A. R.C.S., D.A.: consultant anæsthetist, Royal Masonic Hospital, London.

The Hospital for Sick Children, Great Ormond Street, London:

ATWELL, J. D., M.B. Leeds: house-surgeon.
HOUSTON, I. B., M.B. Manc., M.R.C.P.: house-physician.
MARSHALL, W. C., M.B. Sydney, D.C.H.: house-physician.
PAINTER, PATRICIA, M.B. Lond., F.F.A. R.C.S., D.A.: anæsthetic registrar.

Manchester Regional Hospital Board:

BARNES, K. L., F.R.C.S.: part-time consultant orthopædic surgeon and surgeon-superintendent, Wrightington Hospital, near Wigan.
CROSBY, PAUL, M.B. Bombay, M.R.C.P.E., D.T.M. & H.: assistant chest physician, Nab Top Sanatorium, Marple, Cheshire, and associated chest clinics.
GIBB, G. M., M.B. St. And., D.P.M.: consultant psychiatrist and deputy medical superintendent, Lancaster Moor Hospital.
WOMACK, A. M., M.B. Manc., M.R.C.P.E., D.PATH.: consultant group pathologist, Bury and Rossendale Hospital.

United Manchester Hospitals:

ANSCOMBE, A. R., M.S. Lond., F.R.C.S.: part-time consultant surgeon.
FITZGERALD, T. B., D.S.C., M.B. Birm., F.R.C.S.E., M.R.C.O.G.: part-time consultant obstetrician/gynæcologist.
TORRANCE, H. B., M.B. Edin., F.R.C.S.E.: part-time consultant surgeon.

Obituary

PERCIVAL THOMAS NICHOLLS
K.C.B., F.R.C.S.

As we announced last week, Surgeon Vice-Admiral Sir Percival Nicholls, a former medical director-general of the Navy, died in the Royal Naval Hospital at Haslar on March 1.

He was born in 1877 and qualified from the Middlesex Hospital in 1900. The following year he joined the Naval Medical Service. In 1907 he was awarded the Order of the Crown of Italy for services in the Messina earthquake. He served throughout the 1914–18 war and was made fleet surgeon in 1915. In 1926 he was promoted to surgeon captain. The following year he was appointed principal medical officer at the Royal Naval Barracks, Portsmouth, and in 1927 senior medical officer of the medical section at the Royal Naval Hospital, Haslar. In 1932 he was promoted surgeon rear-admiral and became medical officer in charge of the Royal Naval Hospital at Malta. He was appointed medical director-general of the Navy in 1937 and promoted to the rank of surgeon vice-admiral. He retired in 1941, but in 1942 he returned to duty to take charge of the R.N. auxiliary hospital at Kilmacolm.

A colleague writes:

"Admiral Nicholls was a tall man with a commanding presence. He had a deep feeling of sympathy with his patients, who always received an attentive hearing of all their troubles. Outside his professional work he made a mark by playing tennis for the Navy as a captain. He had a happy family life; and in this warm environment young officers were welcomed and made to feel at home."

Admiral Nicholls was appointed C.B. in 1934 and K.C.B. in 1939. He was elected F.R.C.S. as a member of 20 years' standing in 1940. He leaves a widow and two daughters.

PHILIP HAMILL
M.A., M.D. Cantab., D.Sc. Lond., F.R.C.P.

Dr. Hamill, who died on March 4, was for many years lecturer in pharmacology at St. Bartholomew's Hospital and, after his retirement, the General Medical Council's visitor in pharmacology. But he never lost his interest in clinical medicine, and he served on the staff of the Metropolitan Hospital, where he was senior physician when he retired.

He was a scholar of St. Paul's School and a major scholar of Trinity College, Cambridge, and was placed in the first class of both parts of the natural sciences tripos. After taking his B.A. in 1906, he stayed in Cambridge for another two years as a Coutts-Trotter research student, working in the Physiological Laboratory and, under Prof. W. E. Dixon, in the Pharmacological Laboratory. He entered St. Bartholomew's Hospital with a scholarship in 1909 and qualified in 1910. The same year he took the D.SC. Lond., and the following year he was awarded the Raymond Horton-Smith prize for his Cambridge M.D. thesis. He was a junior demonstrator of pathology at Barts until he went to Mesopotamia with the R.A.M.C. in 1916. There he unfortunately contracted malaria and dysentery, and he was invalided to India where he remained until the end of the war. When he was demobilised in 1919 it was clear that his illnesses had left their mark. He returned to his old love, pharmacology, and became a part-time lecturer at Barts. A colleague remembers him as a very good teacher, and recalls that the students appreciated his somewhat impish humour and his excellent demonstrations which always "showed what they were supposed to do". In addition to his appointment at the Metropolitan Hospital, Hamill became a consulting physician to the London County Council in 1930, and he served at St. Andrews', St. Nicholas, and St. Leonard's Hospitals.

Besides his work as a teacher and clinician he shared in the administration of his specialty. He was an examiner in pharmacology for London and Cambridge Universities and a member of the Therapeutic Trials Committee of the Medical Research Council. He was secretary to the Pharmacopœia Committee of the General Medical Council, and after he had retired from his hospital appointments he visited all the medical schools to inspect the teaching of pharmacology for the Council. Under the National Health Service he proved himself a valuable member of a London hospital management committee. He was insistent that the hospital secretaries and pharmacists should have a say in the quality of goods and drugs for their hospitals.

N. G. H. writes:

"Dr. Hamill's equable and cheerful enthusiasm did much to promote harmony amongst his colleagues and loyalty in his juniors. Though a leading expert on pharmacology he always insisted that a patient's diet should be prescribed first and the drugs afterwards. In the days of the voluntary hospital service, he ensured that the Visitors of King Edward's Hospital Fund were able to report that the patients at 'The Met.' were among the best fed in the country. Hamill supported the National Health Service, feeling that much might be made of the union of the voluntary and L.C.C. hospitals, to both of which he had given so much of his time. His impressive figure and fund of anecdote will be much missed."

CYRIL CUTHBERT BARNARD

B.A. Lond., F.L.A.

Mr. Barnard, librarian to the London School of Hygiene and Tropical Medicine, was killed in a road accident on March 6 at the age of 64.

He was educated at the Stationers' Company's School, Stroud Green, and in 1922 he graduated B.A. with honours in German as an external student of the University of London. He also held the university diploma in librarianship and was a fellow of the Library Association. In 1913 he was assistant at the Reform Club library, in 1914 assistant at the library of the Royal Society of Medicine, in 1918 assistant librarian at the Wellcome Historical Medical Museum, and in 1921 he was appointed to the post he still held.

At the London School of Hygiene and Tropical Medicine he organised and built up a library worthy of that great teaching and research institution. He found existing systems of classification unsuitable for the quick and easy reference he desired, and he devised a system which he published in 1936 as *A Classification for Medical Libraries*. This system was adopted in a number of British and foreign libraries, including that of W.H.O.

C. W. writes:

"Barnard was a scholar—a linguist and a historian—well versed in the humanities. He was a prominent member of the Society of Friends, and he had all the charity which that Society encourages. His figure was small and slight, and in recent years his health had not been good; his character suited his frame, for he was modest, though behind the unobtrusive manner and the kindly generosity of his nature there existed a high degree of firmness of moral purpose which showed itself in his quiet but inflexible stand against war at a time when pacificism was not popular. There was humour also, and I remember a delighted chuckling laugh when it was provoked in my room the day before he died."

Mr. Barnard leaves a widow, a son, and a daughter.

The photograph of Mr. W. J. Stuart which we reproduced last week (p. 527) was by Yerbury, Edinburgh.

Notes and News

PROGRESS IN DENTISTRY

Guy's Hospital Dental School held another of its annual clinical meetings last Saturday. The year since the last one has seen no dramatic advances in dentistry but a steady progress in the scientific approach to many of the basic problems. Like other dental teaching hospitals, Guy's now places rather less emphasis on the purely mechanical aspects of dental prosthetics, and more on the clinical difficulties of producing efficient, comfortable, and pleasing-looking dentures—a thing which, in spite of all efforts to reduce the ravages of dental caries, will inevitably form a large part of dental practice for many years to come.

The National Health Services has to spend many thousands of pounds each year on repair of dentures, and Mr. D. J. Neill has made a small-scale investigation into the causes of their breakage. Much can be done by instructing the patient in the better care of his dentures; for there is too great a tendency to think of the acrylic resins as being almost unbreakable. Mr. Neill also drew attention to certain faults in denture design which dispose to early mechanical failure.

The high-speed air turbine drill is rapidly becoming an established feature of the dental surgeon's equipment. The air turbine has had its teething troubles, but these have been largely overcome, and its future seems much brighter than that of the "airbrasive" instrument which appeared (and disappeared) a few years go.

Mr. W. A. Vale demonstrated its use in the easy and relatively painless preparation of large cavities, and Mr. J. P. I. Rose was able to show, by means of a vibration-measuring device connected to a cathode-ray oscilloscope, that the amplitude of the vibrations felt by the patient was reduced by a factor of about forty.

Great use is being made of colour photography, both for teaching and for recording interesting cases. During the morning session, Mr. A. R. Thompson presented a short and beautifully made film of his method of root resection under a general anæsthetic.

Mr. P. A. Long arranged a particularly topical exhibit on the hazards of ionising radiations, and it was interesting to note that much greater screening is now provided in the X-ray department for the protection of the radiographers, and of the patients when more than one X-ray machine is in use at the same time. Although the radiation received by the gonads during a dental X-ray examination is very small, it must be remembered that the cervical lymph-nodes, and the marrow of the mandible and adjoining bones, receive a very much larger dose. The advice is now given that the fastest possible films should be used, that the diaphragm in front of the tube should be as small as possible, and that the beam should be filtered by 2 mm. of aluminium. All new apparatus incorporates this filter, but there must be many older machines in use without it.

There has been a great revival of interest in the treatment of dead teeth by means of root-canal fillings—a subject which has now received the name of "endodontia"—and an exhibit by Mr. A. H. R. Rowe and Mr. W. C. McLachlan showed some of the more recently developed techniques.

The vexing problem of the "dry socket" has been investigated in the casualty department and, despite much careful work, its ætiology remains rather mysterious. Keeping the saliva away from the socket until a firm blood-clot has formed seems one of the best methods of prevention, and packing with zinc oxide and oil of cloves provides the best treatment. Antibiotics appear to be of little value either for prevention or for treatment.

In the afternoon, Prof. M. A. Rushton gave his annual and always popular talk on cases of interest referred to his department during the year. At present, he is making a particular study of congenital enamel dysplasias and hypoplasias. He also discussed the many cases seen of sore and hyperæmic palates under artificial dentures. In his view, this condition is only rarely caused by a tissue reaction to the material of the denture, and is far more likely to be the result of an iron-deficiency

anæmia—although there is always a possibility that it may be produced by a too literal adherence to the instructions of the dental surgeon always to sleep with the dentures in place, especially if this policy is carried out for a number of years, and is associated with infrequent cleaning of the plate.

University of St. Andrews

A combined clinical and medical sciences course will be held at Queen's College, Dundee, from October, 1959, to March, 1960. Further particulars may be had from the dean of the faculty of medicine, at the university.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting on March 2, with Mr. Arthur Jacobs, the president, in the chair, Chit Sein was admitted to the fellowship of the Faculty *qua* physician.

Scottish Conjoint Board

The following have been granted the licence of the Royal Colleges of Physicians and Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow:

Abdullah Saleh Affara, Gabor Antony, M. J. Carter, Mohammed Moosa Choonara, G. Ialomita Constantinescu, Janos Derjanecz, Magdolna Erdohazi, Ferencz Sandor Freisinger, Laszlo Iffy, I. B. Krinitzky, J. R. Lorenz, R. E. M. Macdonald, Zoltan Mera, George Meszaros, Noel Omar Mohammed, Margaret E. Pawson, H. S. M. Perera, E. J. Pick, J. Tharmasingam Ponnampalam, Raymond Randall, Theresa Sebestyen, Anthony de Toszeghi, Anne M. Urquhart, Apollonia B. Weber. Dragana White.

Postgraduate Medical School of London

A symposium for consultant pathologists on the staphylococcus will be held from July 15 to 17 at this school, Ducane Road, W.12. Further particulars will be found in our advertisement columns.

Ophthalmological Society of the United Kingdom

The annual congress of this society will be held from April 9 to 11, at 1, Wimpole Street, London, W.1. The programme will include the presidential address by Mr. R. C. Davenport on facets of glaucoma, the Bowman lecture by Prof. Louis Paufique on the present status of the treatment of the retinal detachment, and symposia on the treatment of ocular injuries and the swollen optic disc. Further particulars may be had from the hon. secretary of the society, 47, Lincoln's Inn Fields, W.C.2.

Association of Industrial Medical Officers

This association will hold a meeting on March 20 and 21, at the London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1, and St. Thomas's Hospital, S.E.1. Further particulars may be had from the association, 47, Lincoln's Inn Fields, W.C.2.

Institute of Dental Surgery, London

Prof. R. V. Bradlaw has been appointed director of studies of the institute and director of the Eastman Dental Hospital in succession to Prof. F. C. Wilkinson, who is retiring later this year.

Anti-infectious and Antimitotic Chemotherapy

The first international symposium on this subject will be held on Sept. 12 and 13 in Geneva. The president is Prof. G. Bickel, director of the medical clinic of the University of Geneva, and further particulars may be had from Dr. P. Rentchnick, Case Stand 471, Geneva.

A meeting of the Biochemical Society will be held on Friday, March 20, at 11 A.M. On Saturday, March 21, the society is to hold a joint meeting with the Association of Clinical Biochemists at 10.30 A.M. Both meetings will be held at the Department of Biochemistry, South Parks Road, Oxford.

The title of fellow of University College London has been conferred on Dr. Howard Nicholson.

During April and May Sir Francis Walshe will be in the United States, acting as visiting professor of neurology in the medical schools of St. Louis, Cincinnati, and San Francisco.

An award of the Langley prize (£21) will be made this year. Entries, from past or present officers of the West African medical departments, of either published or unpublished work must reach the Dean, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, not later than Oct. 1.

The *Lancet* award for the best series of prints published by a member of the medical group of the Royal Photographic Society in the medical press during 1958 has been awarded to Dr. W. Hewitt and Mr. A. L. Wooding, of St. Thomas's Hospital Medical School, London.

The spring dinner of the Wessex Rahere Club will be held at the Royal Clarence Hotel, Exeter, on Saturday, April 18. Membership of the Club is open to all Barts men practising in the West Country. The hon. secretary is Mr. A. Daunt Bateman, 11, Circus, Bath.

Jill and Johnny go to Hospital is the title of a painting-book which the League of St. Nicholas is now sending to the small patients of Westminster Children's Hospital before they are admitted.

Diary of the Week

MARCH 15 TO 21

Sunday, 15th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
10.15 A.M. Mr. Maxwell Ellis: Common E.N.T. Conditions.

Monday, 16th

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Prof. T. B. Counihan: Treatment of Cardiac Œdema.
HUNTERIAN SOCIETY
8.30 P.M. (Talbot Restaurant, London Wall, E.C.2.) Dr. L. G. Norman, Dr. R. S. F. Schilling: Emergence of Industrial Medicine.
UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. H. B. Goodall, Dr. William Walker: Genetic Factors in Blood Diseases.

Tuesday, 17th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. M. O. Skelton: Pathological Lesions of the Adrenal Gland. (Erasmus Wilson demonstration.)
ST. MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W.2
5 P.M. Mr. Aleck Bourne: Clinical Significance of Amenorrhœa.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. C. M. Ridley: Dermabrasion.

Wednesday, 18th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
4 P.M. Dr. Langton Hewer: Forty Years On. (Frederic Hewitt lecture.)
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.15 P.M. *Endocrinology, General Practice.* Prof. E. J. Wayne, Dr. David Wheatley, Dr. A. G. Macgregor, Dr. D. N. Baron: Diagnosis of Thyroid Disease.
POSTGRADUATE MEDICAL SCHOOL
2 P.M. Prof. J. W. Howie: Steam Sterilisation.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. N. S. Plummer: Pulmonary Tuberculosis Before Chemotherapy.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. J. T. Ingram: Seborrhœic Diathesis.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. H. K. Snell: Work of the Prison Medical Service.
HARVEIAN SOCIETY OF LONDON, 11, Chandos Street, W.1
8.15 P.M. Prof. E. B. Chain: Recent Studies in Carbohydrate Metabolism. (Harveian lecture.)
EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Dr. R. W. Parnell: Physique and Family Structure.
NORTH WESTERN THORACIC SOCIETY
5 P.M. (Aintree Hospital, Liverpool.) Mr. Leslie Temple: Surgery of Pulmonary Tuberculosis—Experience since 1950.

Thursday, 19th

ROYAL SOCIETY OF MEDICINE
4.45 P.M. *Dermatology.* Dr. Sybil Horner, Dr. Geoffrey Hodgson, Dr. D. K. Harris, Dr. A. J. M. Johnston: New Industrial Hazards.
BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Dr. D. A. Wilson: Aspects of Health and Safety.
HYPNOTHERAPY GROUP
8 P.M. (1, Wimpole Street, W.1.) Mr. Maurice Susman, Mr. E. E. Wookey, Dr. Denys Kelsey: Hypnosis in Surgical and Dental Anæsthesia.
MANCHESTER MEDICAL SOCIETY
8 P.M. (Staff House, University of Manchester.) Dr. G. J. C. Brittain: The Use of the Postoperative Recovery Ward.
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Mr. K. W. Monsarrat: The British Hospital Service—Past and Present. Dr. T. L. Hughes: Administrative Problems of the Present National Health Service.

Friday, 20th

ROYAL SOCIETY OF MEDICINE
5.30 P.M. *Epidemiology and Preventive Medicine.* Dr. B. P. Marmion: Q Fever—Recent Developments and Some Unsolved Problems. Dr. T. T. Baird, Dr. A. D. Evans: An Interim Account of an Autumnal Epidemic of Q Fever in Cardiff.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Mr. William McKenzie: Advances in the Treatment of Deafness.
5.30 P.M. Dr. A. C. Thackray: Salivary Gland Tumours of the Palate.